SYMPOSIUM ON THROMBO-EMBOLISM

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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

EDITORS

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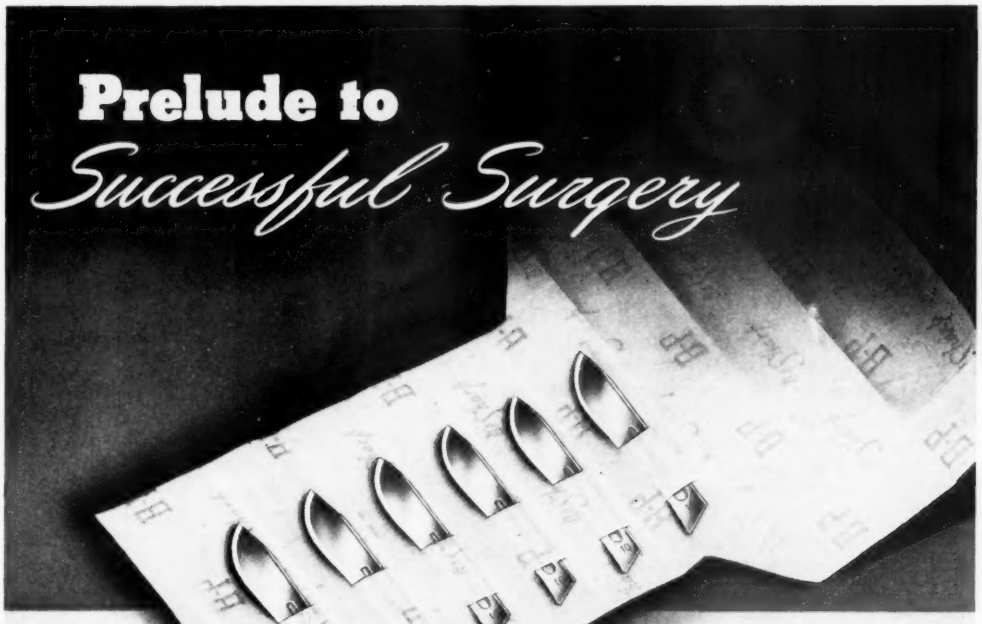

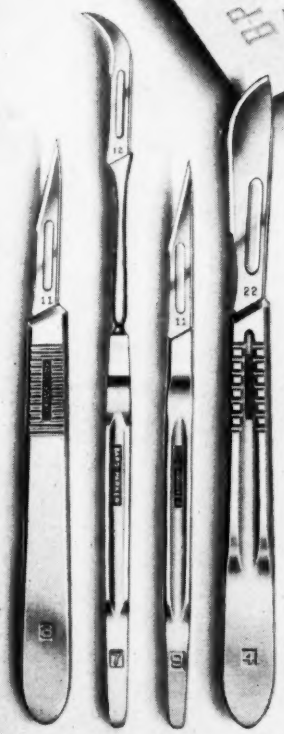

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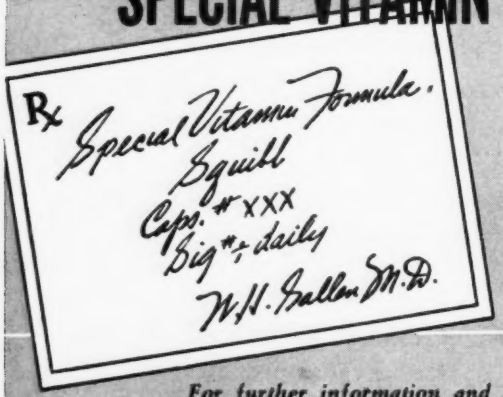

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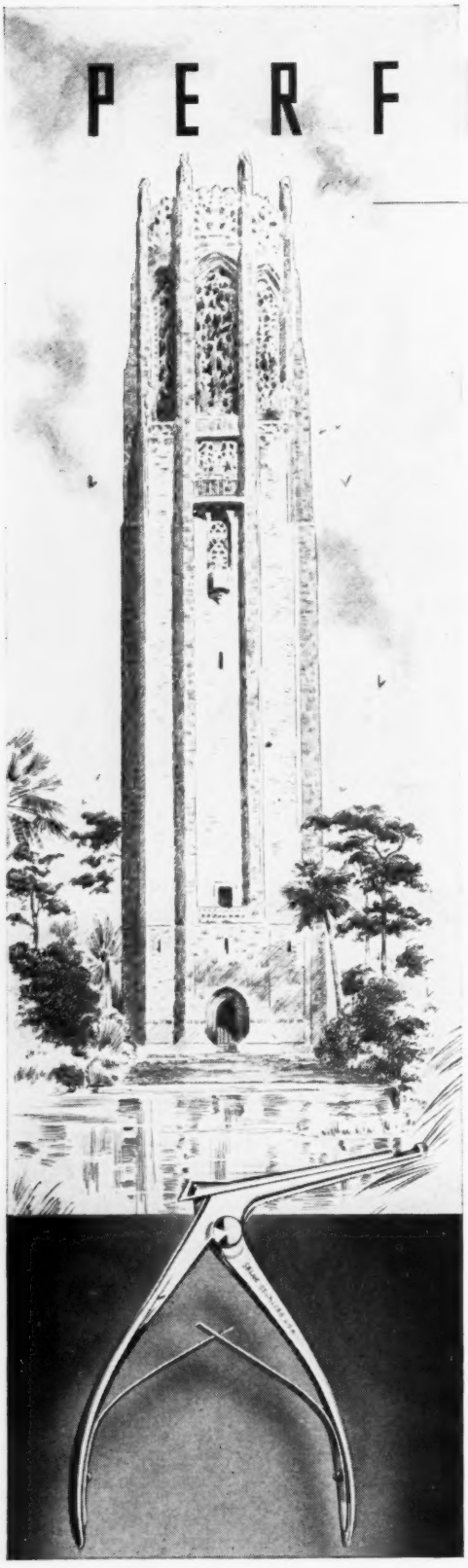

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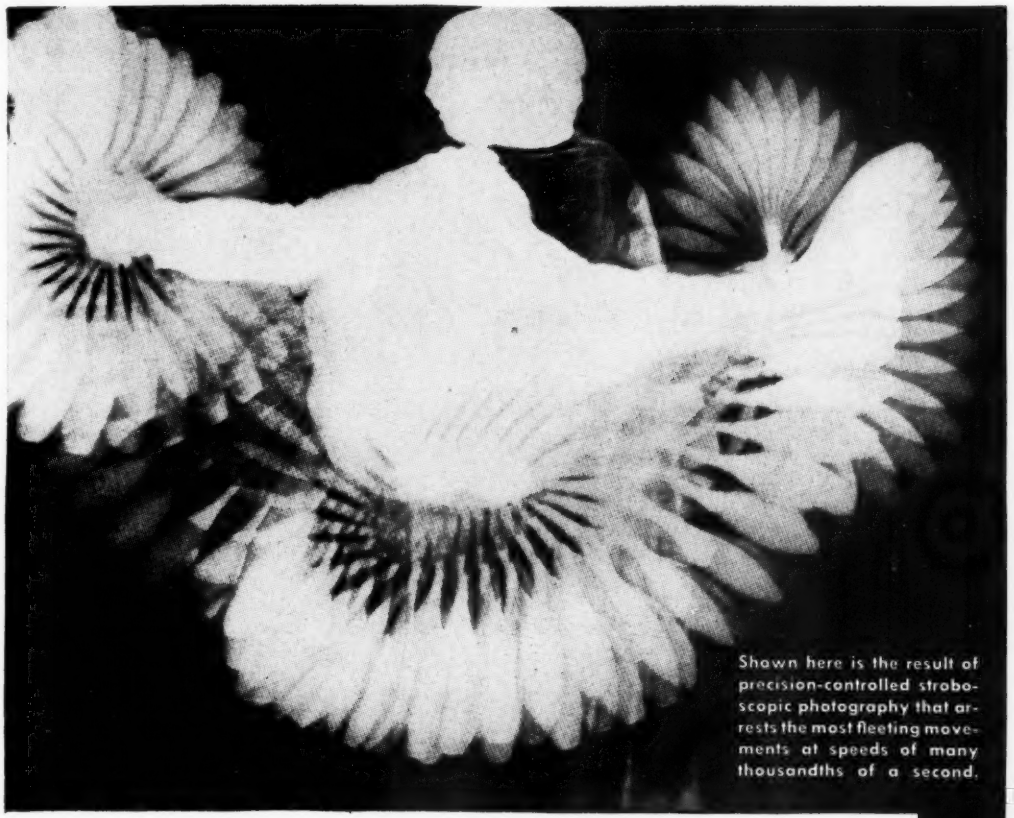

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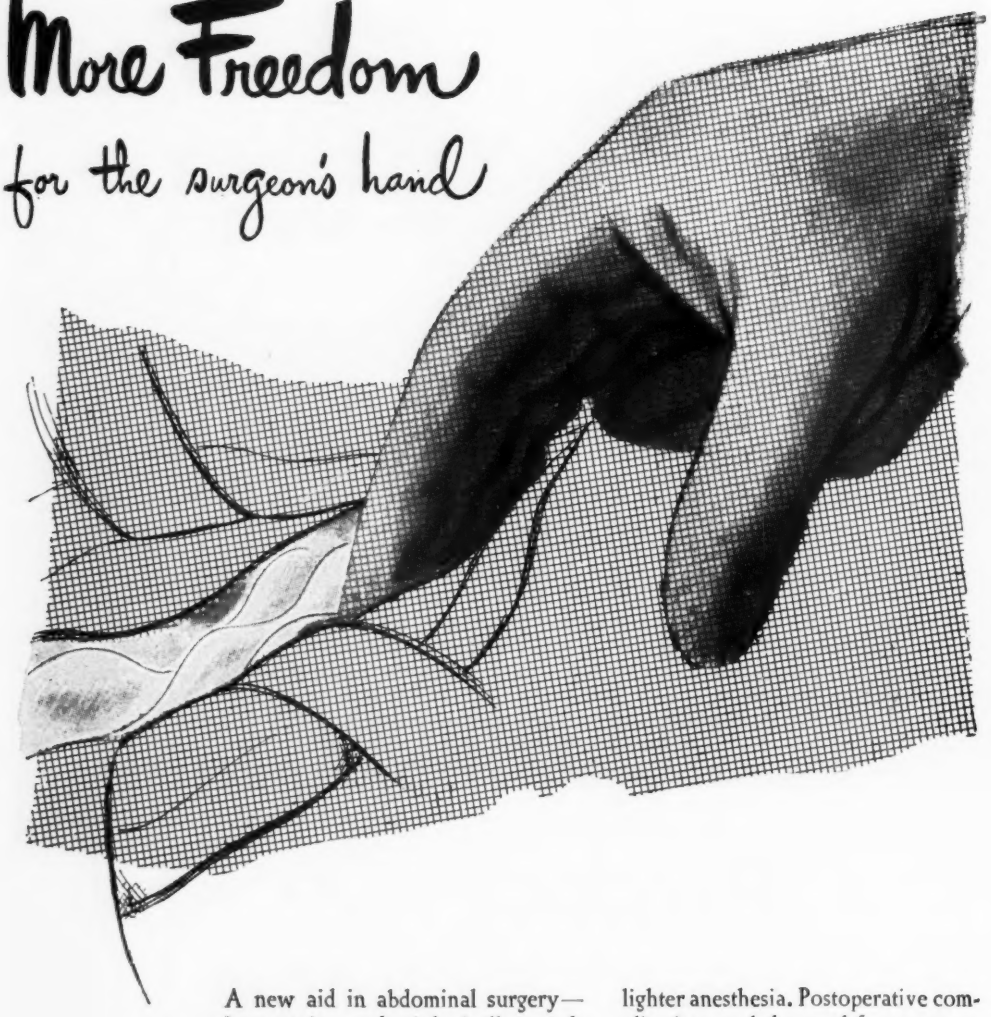

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*Reznikoff, P. and Goebel, W. F.: J. Clin. Investigation 16:547, 1937.

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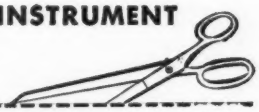

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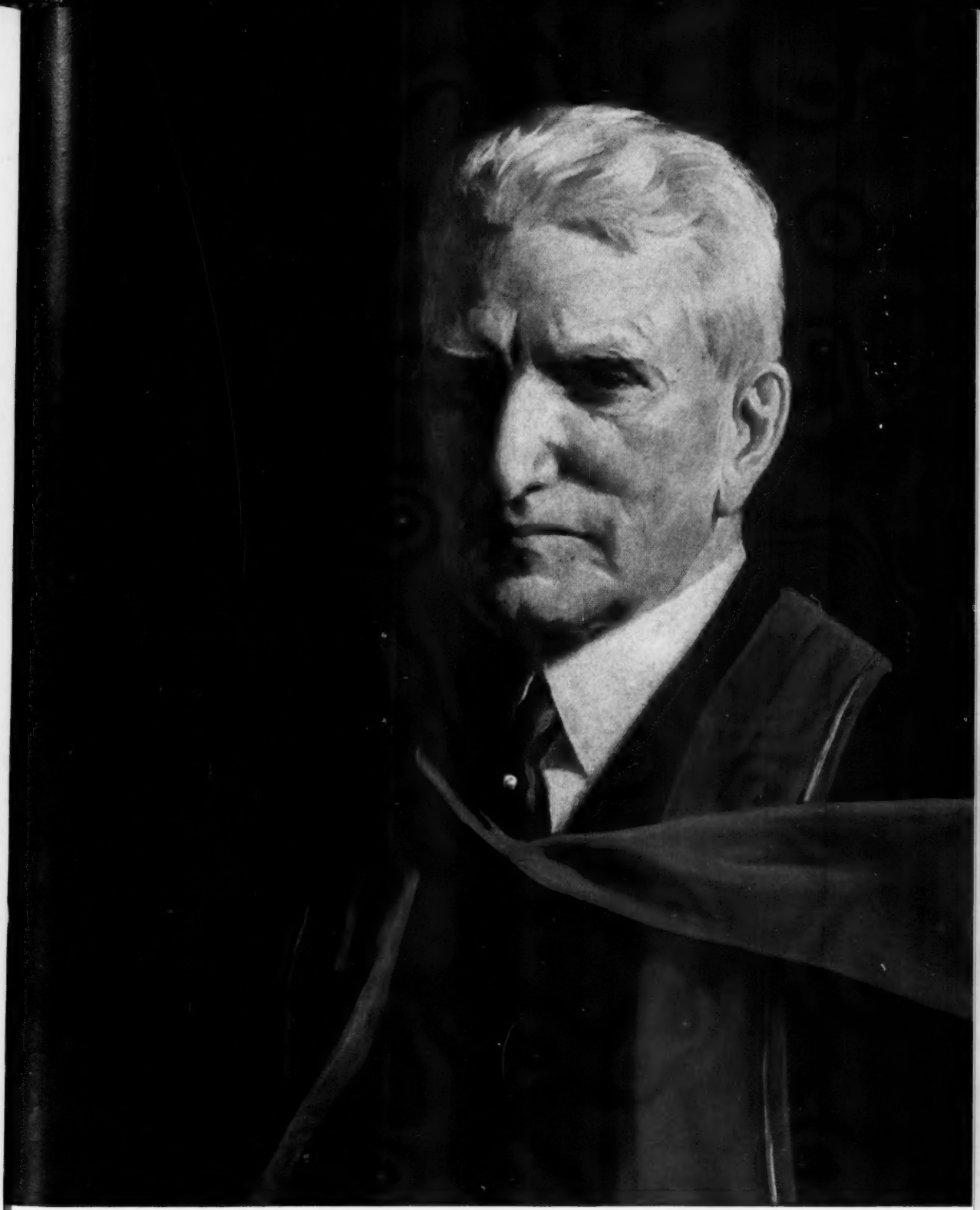

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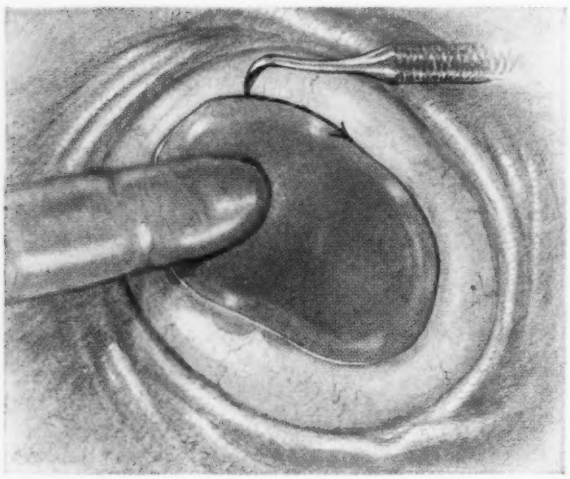
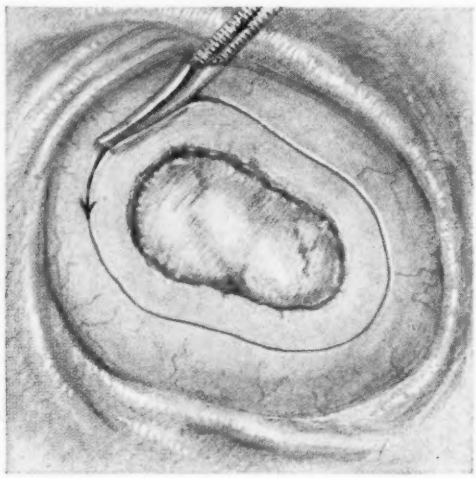
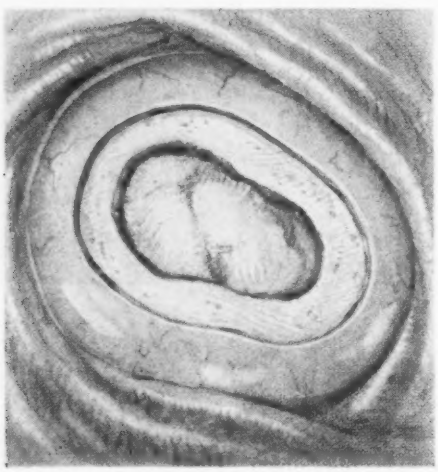


1. A tantalum plate of correct size and shape is placed over the defect and outlined by a scriber.

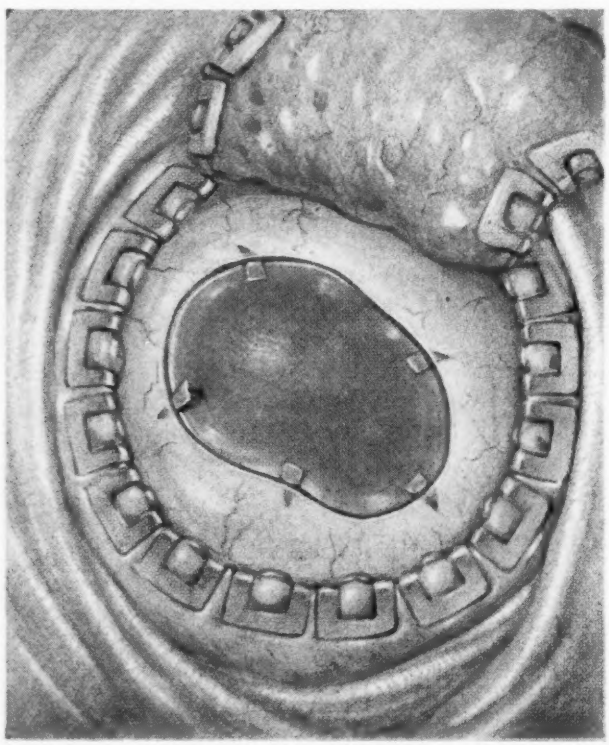


2. A lineator with cutting edge cuts the outer skull table, following the plate outline.

Skull Repair



3. A shelf is formed by chiseling away a thin layer of outer skull table from edge of defect to groove cut by lineator.



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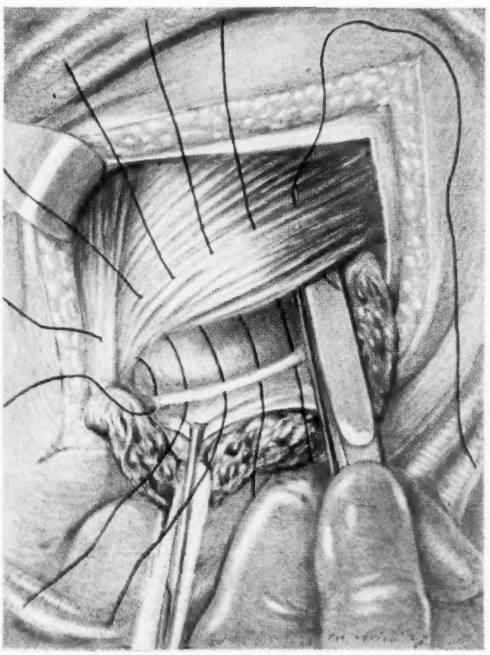

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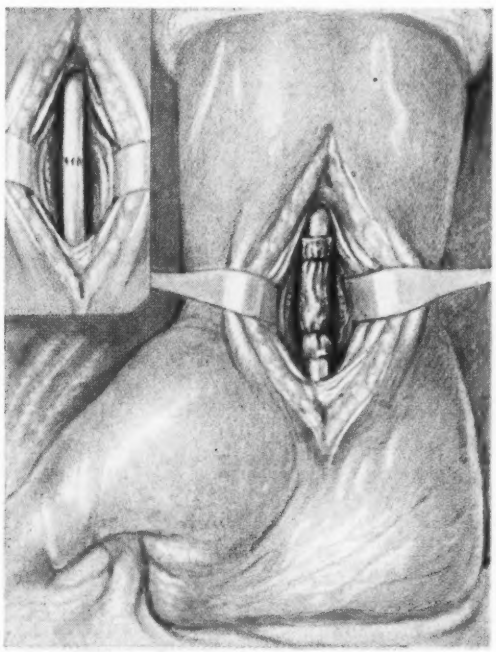
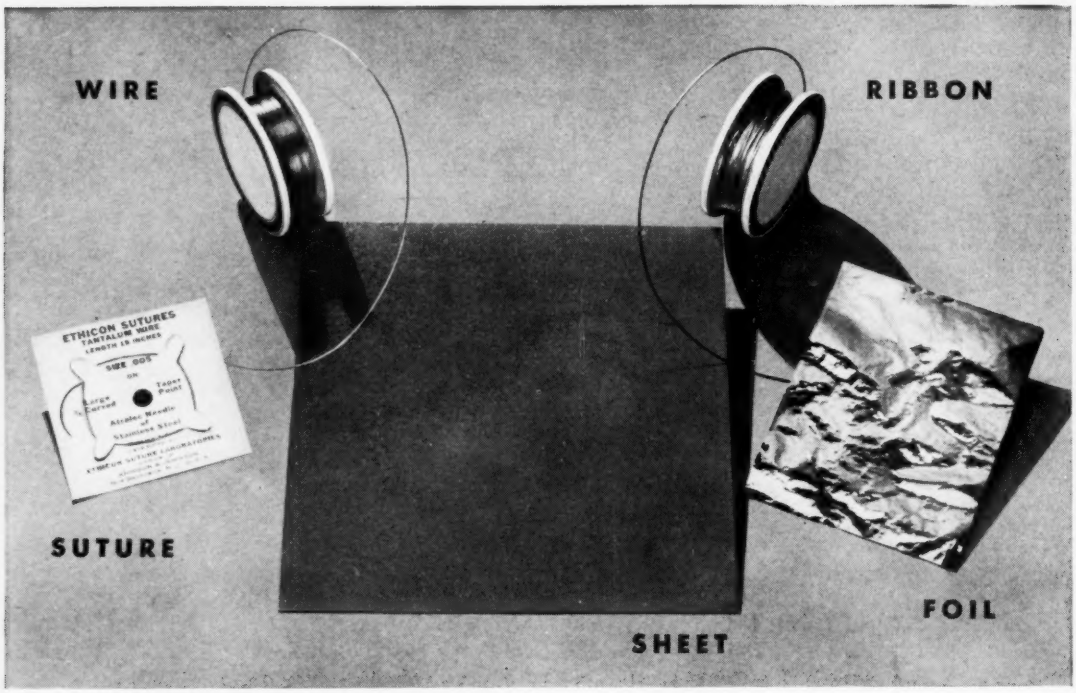


Nerve Repair

(Inset) Fine gauge tantalum sutures approximate epineurium of severed median nerve... Tantalum foil wrapped loosely about repaired section and secured by loose ties.



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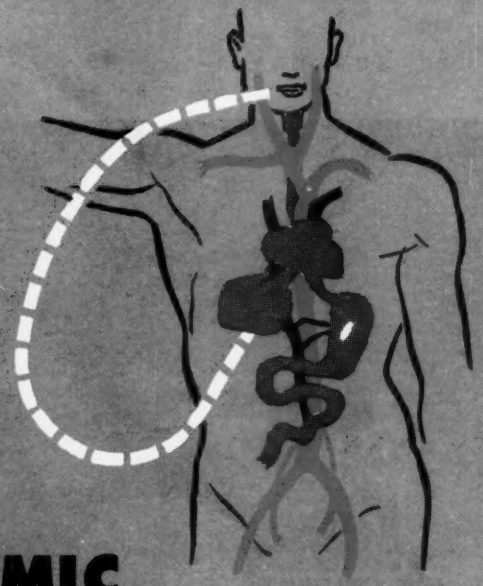

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Long route through portal system to general circulation

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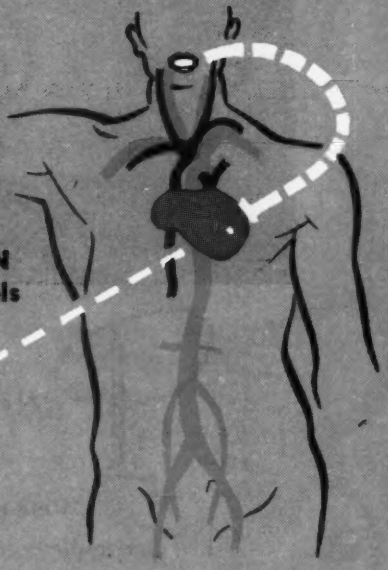

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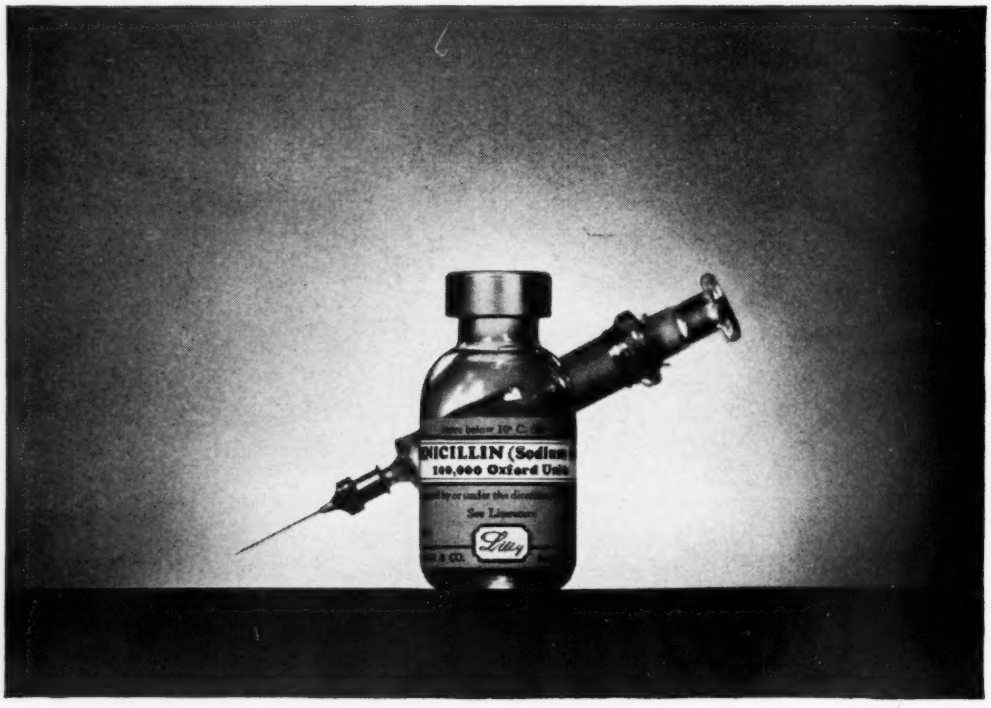

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SURGERY

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Original Communications

Symposium on Thrombo-Embolism

THE PROBLEM OF THROMBO-EMBOLISM

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THE formation and propogation of thrombi in the vascular tree confronts one with many questions. The literature on this subject is very extensive; we have annually reviewed it elsewhere.[1] The purpose of this communication is to describe briefly the methods of diagnosis and treatment which have been gradually developed as a result of our own experience. This discussion will be limited to the peripheral venous system and the pulmonary arterial tree. Arterial thrombi and emboli have been discussed previously.[2]

THE LOCALIZATION OF THROMBI

The primary source of thrombi in the venous system is not always obvious. The clinical importance of the thromboses in the lower extremities and the pelvis is so great that one need simply mention the thromboses in the upper extremities as being comparatively infrequent and brought on either by trauma, as the axillary thrombosis of effort, or following axillary dissection, as a carcinomatous periphlebitis, or following intravenous injections or infusions. The majority of thrombi, however, form in the lower extremities and the pelvic veins. It is not sufficiently recognized that from 50 to 60 per cent of all adults carry thrombi in the plantar veins or veins of the calf muscles,[3] that phleboliths are often seen in the x-ray films of the pelvis, and that the broad ligament frequently carries plugged veins transected during hysterectomies.[4]

We are grateful for the co-operation of Dr. N. C. Gilbert, Dr. G. K. Fenn, and Dr. G. W. Scupham of the Department of Medicine, Dr. E. L. Jenkinson of the Department of Roentgenology, and Dr. E. F. Hirsch of the Department of Laboratories, St. Luke's Hospital, Chicago.

Received for publication, Aug. 21, 1944.

It has been customary since the teachings of the older pathologists to regard *slowing of the circulation, changes in the vessel wall,* and *increased coagulability of the blood* as the three factors responsible for thrombosis.

Slowing of the Circulation.—This factor alone will hardly ever suffice to produce thrombosis. Blood may stay fluid between two ligatures if

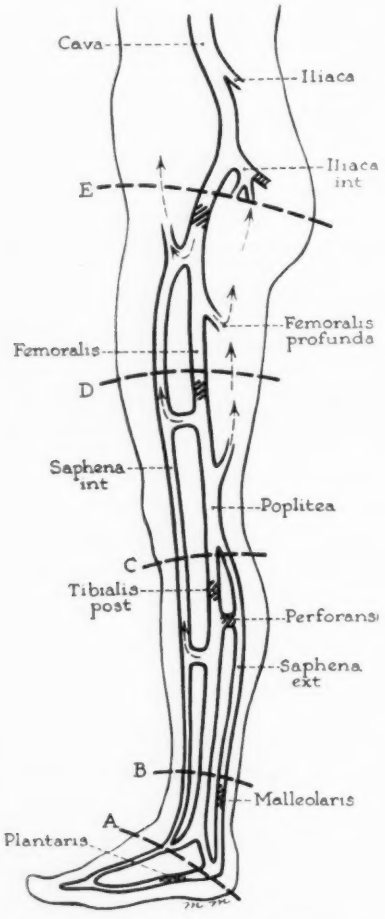

Fig. 1.—The primary sources of deep venous thrombosis in the lower extremity. Mechanical obstructions localize such thrombi to certain segments. *A*, Tendon of peroneus longus crossing plantar vein; *B*, upper margin of malleolar ligament; *C*, upper edge of soleus muscle; *D*, adductor canal; *E*, inguinal ligament.

care is taken not to injure the intima, but when other factors are present it will serve to localize the clot to a certain segment. The postoperative state and the prolonged bed rest of the cardiac with slow circulation times predispose to thrombosis; the constricting action of ligaments, tendinous insertions, and bony prominences may determine the segmental localization of the thrombi (Neumann[3]). (See Fig. 1.) Obviously, however, since such constrictor and compressing influences operate in all of us, they do not suffice alone to produce clotting.

Injury to the Intima.—Mechanical trauma, such as tearing, crushing, or stretching a vessel, operates in many cases of thrombosis following fractures, sprains, gunshot, and stab wounds. The vessel itself does not have to be directly injured. Many ankle sprains, fractures of the lower leg, knee, and pelvic injuries are seen daily which start a thrombus at the site of injury. Infections such as occur in bacterial endocarditis, typhoid fever, pneumonia, or scarlet fever may localize to the intima of a peripheral vessel, producing a raw surface and a deposition of platelets.* The vessels may also be sensitized to allergens, producing damage.[5] Ulceration of an atheromatous plaque in the aorta produces thrombosis. Aneurysms invariably harbor thrombi.

Increased Coagulability of the Blood.—There are many states in which the blood clots more readily. Any trauma which liberates thrombokinase from the tissues will do so; this occurs after massive injuries to muscle and after any major operation. Loss of plasma in burns and shock, dehydration due to vomiting, or rapid diuresis after mercurials produces hemoconcentration and increased viscosity. Patients with polycythemia or those suffering from carcinoma also have a tendency to blood-clotting, possibly because of rapid destruction of platelets which liberate thrombokinase in the former, and because of tissue destruction in the latter.

PROPHYLAXIS OF THROMBOSIS

What are the measures one can employ to minimize the operation of these factors? In combating the retardation of blood flow, most surgeons are cognizant of the importance of early mobilization of patients. It can be statistically proved that prolonged immobilization of an identical group of patients will lead to a higher incidence of thrombi and emboli. But obviously many patients cannot be mobilized for eight to twelve weeks, for example, those suffering from severe abdominal infections or fractures at certain sites. Elevation of the foot of the bed on chairs or on shock blocks is an excellent, simple procedure to accelerate venous return from the lower extremities. The pelvis must be included in this reversed drainage (Figs. 2 and 3). Years ago we advocated a stationary bicycle attached to the patient's bed but this can be easily substituted by having the patients dorsiflex and plantarflex their ankles, which exercises their calf muscles and empties the veins. Naturally all these measures have their contraindications and limitations.

It is difficult to see how one could prevent trauma, whether mechanical, thermal, or bacterial, once it affects the vessel wall; but one can help to localize and prevent the mural thrombus from breaking loose by measures to be discussed presently.

The interest in preventing *excessive coagulability of the blood* has arisen since the advent of purified and comparatively nontoxic anticoagulants.[6] In order to use such drugs preventively and not only

*Atypical (virus) pneumonia seems to predispose to clotting.

therapeutically, it became necessary to look around for a simple diagnostic test which would detect early changes in the clotting mechanism. The customarily employed tests of clotting time and bleeding time do not reveal any clear-cut changes. Prothrombin time determined on diluted plasma does detect a tendency toward increased clotting but the method requires skilled laboratory technique.[7] The response of such patients

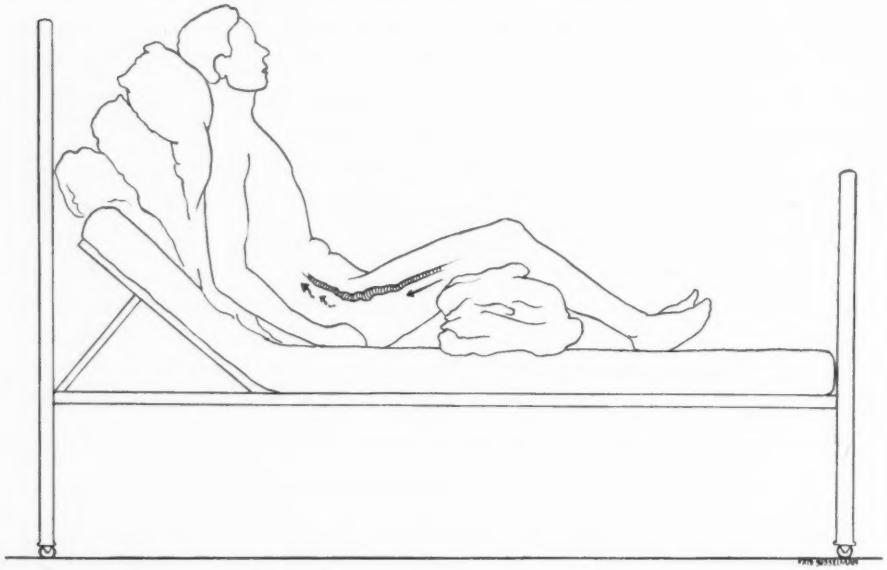

Fig. 2.—Pooling of blood in the popliteal fossa and in the pelvis during the customary Fowler's position. (From de Takats, G., and Jesser, J. H.: Pulmonary Embolism, J.A.M.A. **114**: 1415, 1940.)

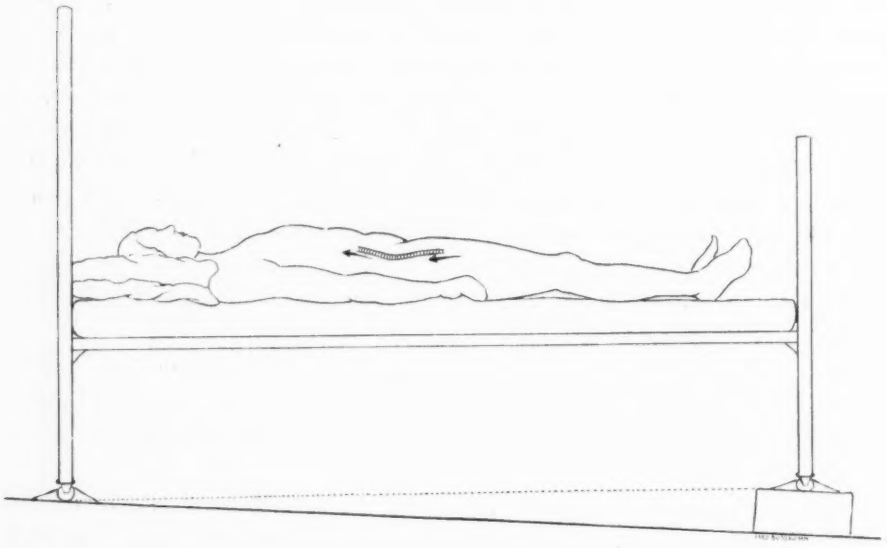

Fig. 3.—Much better venous drainage is accomplished by the Trendelenburg position. The circulation time from foot to tongue is demonstrably accelerated. The foot of the bed is elevated and not the lower leg alone. (From de Takats, G., and Jesser, J. H.: Pulmonary Embolism, J.A.M.A. **114**: 1415, 1940.)

to heparin is strikingly diminished and this decreased heparin tolerance has been used extensively for determining the increase in clotting factors. Such factors have been shown to exist in the postoperative state, in Buerger's disease, and in the presence of any kind of intravascular clotting.[8a] Other factors such as neurogenic influences[8b] and the thromboplastic properties of digitalis[8c] have been investigated. Conversely, drugs like prostigmine[8b] or sulfur compounds [8d] seemed to decrease the increased clotting factors. It has been found practical to determine the heparin response of such patients, who were either suspected of harboring thrombi or who have shown previous evidence of thrombosis. One cubic centimeter (10 mg.) of heparin is injected intravenously. Coagulation times are determined with a capillary tube before ten, twenty, and thirty minutes after the injection of heparin. A flat tolerance curve indicates the presence or imminence of thrombosis (Fig. 4). The normal response can be restored by heparin, by dicoumarol, by sulfur compounds, or by prostigmine.[8] Patients sensitized to heparin can be detected.[8a]

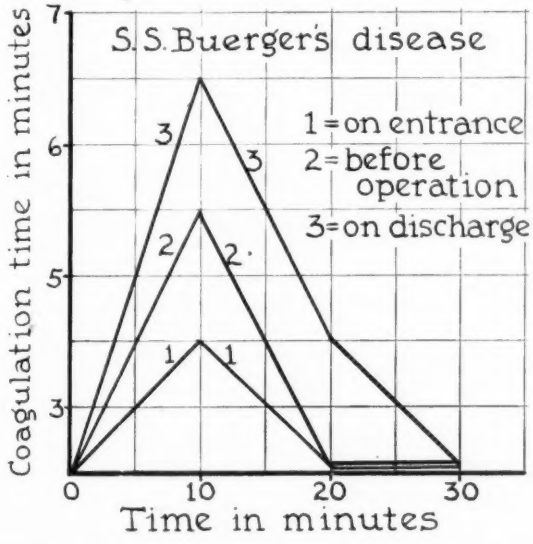

Fig. 4.—Three heparin-tolerance curves of the same patient, indicating a steady improvement of the clotting mechanism following treatment.

For the prophylaxis of postoperative thrombosis, the following drug therapy is used: In patients who have a pre-existing deep venous thrombosis, or have thrown arterial or pulmonary emboli from the heart, the heparin-dicoumarol combination is used when operations of any sort are necessary. In eighty-one such patients no extension of the clot and no emboli occurred. Three patients had major hemorrhages requiring transfusion. These occurred, however, in the first month of our experience. Three patients, all diabetics, presumably with hepatic damage, showed a marked response to a single dose of dicoumarol, necessitating intensive vitamin K therapy to bring the prothrombin level back to a moderately

subnormal level. Five additional patients had a hematoma at the site of the operation, mostly in the stump of an amputated leg. We shall discuss our present method of controlling the dosage of dicoumarol. It requires continuous watchfulness and should probably be carried out by the medical department, just as the dosage of insulin is regulated in the surgical diabetic. Sodium tetrathionate is used in the intravenous drip after sympathectomies for thromboangiitis obliterans. The dose is 0.6 Gm. to each 1,000 c.c. of salt solution. These patients do show an increased tendency to clotting. They also receive tetrathionate postoperatively until their clotting mechanism returns to normal (Fig. 5).

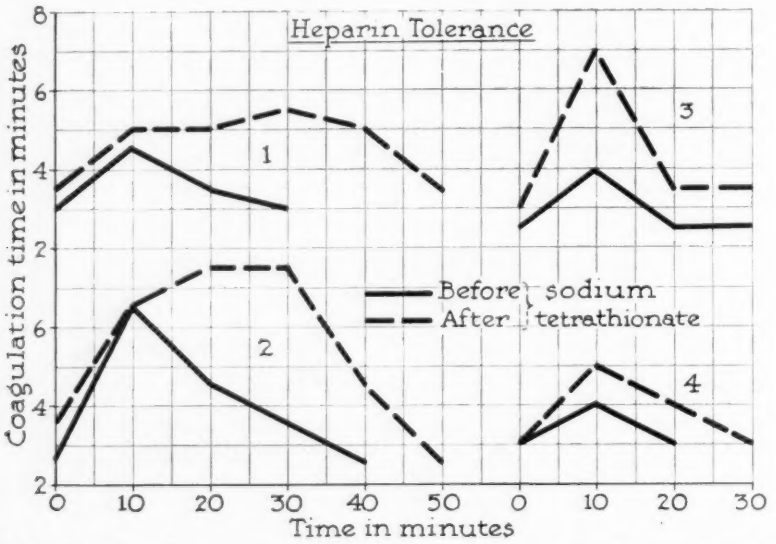

Fig. 5.—Heparin tolerances of four patients all of whom had intravascular clotting. Note that all four developed a better response to heparin. The least response is shown by the patient in Case 4, who had multiple emboli following coronary thrombosis, one of them resulting in gangrene of the left lower extremity. His response to sodium tetrathionate was very small, indicating a marked clotting tendency. (From SURGERY **14**: 663, 1943.)

Prostigmine, which equally seems to improve the patient's response to heparin, is used after all laparotomies, especially pelvic. Its effect on postoperative intestinal and bladder atony has been noted many times. One cubic centimeter of 1:2000 solution is given every four hours, ten times. For some reason, which is not clear, it definitely affects the clotting mechanism.[8b] The exact number of cases in which the prophylactic use of sodium tetrathionate and prostigmine was employed could not be ascertained. It has been employed since July, 1943, to date, on one active surgical and one active gynecologic service in several hundred cases. There was no thrombo-embolism in the group to which it was given.

THE CLINICAL SYNDROME OF VENOUS THROMBOSES

One need not describe the full-blown picture of iliofemoral thrombosis, with the inguinal pain, the massive edema, and the cyanotic hue

of the extremity. It is more important to realize that the iliofemoral segment is never the primary source of thrombosis but is the result of propagation from elsewhere. The following clinical pictures can be segregated from the several hundred cases which our group has studied.

Group 1.—Superficial phlebitis of pre-existing varicosities, ascending toward the groin. No, or very little, edema exists. No spasm in calf muscles is present. Large, red, painful thrombi are visible and palpable.

Migrating phlebitis in male smokers in the absence of varicosities, with no, or beginning, arterial involvement, makes one highly suspicious of Buerger's disease, which is not within the scope of this paper.

Attention should be directed to the not infrequently observed cases in which large superficial varicosities suddenly become thrombosed in the presence of an old deep venous obstruction. When these patients are treated by the usual combination of high ligation and injections the edema will not subside but may increase.

CASE 1.—Dr. A. E., a 72-year-old physician, had a slowly ascending thrombosis involving the entire long saphenous system, without fever and general systemic disturbance. He had varicosities since the age of 16, but had no discomfort except for the annoyance of having to wear elastic support. Only when the thrombus had obviously reached the groin did he consent to an operation.

Dec. 27, 1940, the left saphenous vein was exposed at the groin. There was a soft friable clot in the saphenous bulb which was aspirated and found to extend into the iliofemoral segment. With the use of an eyedropper attached to the suction apparatus, a large number of soft, friable, red thrombi were aspirated from the femoral vein. However, markedly adherent mural thrombi, obviously of earlier date, were also encountered.

Continuous intravenous drip was started with 600 mg. of heparin daily. Fluids were limited to 2,000 c.c.; coagulation time was kept around ten minutes (capillary coagulation time). A large hematoma developed in the wound, which was expressed through a small incision on the ninth day. At this time heparin was discontinued. The patient was discharged on the fourteenth day.

A re-examination six months later revealed a low-grade chronic edema. The veins were still tender and firm in the calf. A few doses of x-ray treatment helped to absorb the periphlebitic exudate. However, permanent elastic stocking is necessary. To date, four years later, he is in excellent health, has remarried, and still practices. Edema persists.

This was one of our first cases of aspiration and extraction. Today, we would be more inclined to ligate the femoral vein instead of aspirating it through the saphenous. Also, the use of continuous administration of heparin has been discontinued.

Note that the acute superficial phlebitis was superimposed on an old deep venous thrombosis. Such cases are comparatively frequent.

Group 2.—Pressure pain over the lateral aspect of the foot,[9] later over the inner malleolus, then over the posterior tibial vein. There is pain or dorsiflexion of the foot.[10] From day to day the clot seems to ascend; the thigh becomes tender and swollen. The femoral artery pulsates more feebly on the affected side but the calf and foot are warmer. The oscillations are increased over the affected side. Embolism is frequent when

the clot is below the knee, rare when typical milk leg is present (6.6 per cent).[11] Embolism often precedes the appearance of the femoral thrombosis. This is the syndrome of *ascending plantar vein thrombosis.* It occurs more frequently in young, ambulatory individuals.

CASE 2.—Mrs. E. V., a 26-year-old graduate nurse, suffered a fissure of the right patella without separation of the fragments, in an automobile accident. A circular cast was applied in a near-by hospital. The sole of the foot began to ache within twenty-four hours. The cast had to be removed in forty-eight hours because of severe pain in the inner malleolus. On arrival at St. Luke's Hospital, six days after the injury, there was slight edema of the right ankle and calf. The lateral aspect of the sole of the foot was tender on pressure. Dorsiflexion produced pain and defensive spasm in the calf muscles. The thigh was not swollen and not tender on pressure.

This patient was treated with anticoagulants only, by a combination of heparin and dicoumarol, for ten days. Her convalescence was uneventful. She wore an elastic hose for three months. No residual edema developed. *This patient could as equally have had a ligation of the superficial femoral vein below the profunda. Since she needed immobilization because of the fracture, only anticoagulant therapy was used. No emboli phenomena occurred in this series of cases.*

Group 3.—No plantar vein involvement is present, but there is ache, cramp, and tightness in calf muscles. There is spasm on dorsiflexion, and increased temperature over the affected calf, with increased oscillations. The femoral vein is not tender; temperature and white count are normal. Emboli are frequent. The process may ascend to the popliteal or femoral vein as in the first group, after which it is less apt to produce emboli. This is the syndrome of calf muscle thrombosis.[10] It occurs more often in the older, immobilized group, but is frequently latent and unrecognized until embolism occurs.

Group 4.—Pain and swelling in buttocks or in adductor muscles close to the inguinal fold occurs. Sciatic neuritis is present. Frequency of urination, mucous diarrhea, or slight suprapubic edema is observed. Palpable cords lateral to the prostate or to the uterus may confirm the diagnosis. An embolus is not infrequent as long as thrombosis is intrapelvic; it is not so likely after extension to the external girdle. This is the syndrome of *pelvic vein thrombosis.*

There are, of course, combinations and transitions from one group to another. Generally speaking, the more latent and bland the thrombus is, the greater its embolizing possibility. In fact, the thrombus is most frequently evident after one pulmonary infarct has taken place.

The role of infectious versus bland thrombi, as discussed by Aschoff,[13] and Ochsner and De Bakey,[14] is not always easy to evaluate. A traumatic or mildly infected thrombus might propagate as a bland, red, nonadherent clot, which breaks loose easily. A bland phleobothrombosis might develop into an inflammatory periphlebitis when it ascends to the inguinal lymphatics, which often harbor infection.

The amount of edema depends on the extent of blocked collaterals,[15] on the extent of the periphlebitic lymphatic obstruction,[16] and on vaso-

spasm.[17] These factors need special attention when planning treatment. They may all be present in the same patient in varying proportions.

METHODS OF TREATMENT

1. *Conservative Treatment.*—For centuries, the swollen milk-leg was immobilized and elevated, the patient being kept in bed for an arbitrary four to six weeks. The edema may be mobilized by mercurial diuretics[18] although our recent studies would indicate that sudden dehydration may lead to increased tendency to clotting, so that the use of diuretics has been abandoned (Table I). The patient must wear a stocking from toes to groin for six to twelve months. That many patients have done well under this management can be best illustrated by Case 3.

CASE 3.—H. J., a 30-year-old woman, developed a left-sided iliofemoral thrombosis at home the twelfth day after childbirth. While at the hospital she complained of cramping in the calf, which was disregarded. When seen at home in 1941, three weeks after delivery, there was a massive swelling of the entire lower extremity. She was told to stay in bed for ten days after the pulse had returned to normal and wear an elastic stocking for six months. Salyrgan was prescribed twice a week. At examination three years later, no trace of edema and no varicosities were found.

TABLE I

THE EFFECT OF RAPID DEHYDRATION ON HEPARIN TOLERANCE (A. W.)

DATE	CONTROL	COAGULATION TIME IN MINUTES			WEIGHT IN POUNDS	REMARKS
		10	20	30		
1/23	3½	5	3½	3½	190	Digitalis, gr. 6, from 1/21 to 1/24
1/25	3½	6	3½	3½	188	Digitalis, gr. 1½, daily until 2/10
1/26	3½	6½	5	3½	186	Mercupurin, 1 c.c.
1/27	3½	4½	3½	3½	175	
1/28	3½	5	3½	3½	168	Lost 18 lb. of fluid in 2 days
1/29	3½	4½	3½	3½	166½	
1/30	3½	4½	3½	3½	166½	
2/ 1	3½	3½	3½	3½		Irrational
2/ 2	3½	3½	3½	3½		Mercupurin, 1 c.c.
2/ 3	3	3	3		156	Lost 11 lb. of fluid; irrational and
2/ 4	3	3	3		154	incontinent
2/ 6	3	3	3		148	
2/ 7	3	3	3		148	
2/ 8	3	3′45″	3		150	
2/ 9	3	3	3			
2/10	3	3	3		156	Digitalis stopped

Criticism of the Method: The difficulty is that the residual edema and the possibility of embolism are entirely left to chance. If the clot is not too extensive, the swelling will be negligible, especially if elastic support is worn for a long time. Immobilization is long and the loss of time is great. The danger of embolism, if the femoral segment is occluded, is small, but the process may involve the other extremity in approximately one-third of the cases.

2. *Anticoagulant Therapy.*—If one lays stress on the danger of the propagation of the clot and the lack of fixation of the most recently

formed red thrombus, the use of anticoagulants seems indicated. Heparin is given at four-hour intervals in 50 mg. doses undiluted, intravenously. While this will not maintain a steadily elevated coagulated time, it is simpler for the patient and its protective value is equally efficient. Simultaneously, oral administration of dicoumarol is started, 300 mg. the first, and 200 mg. the second, day. Prothrombin levels must be determined daily (Fig. 6). The level must be kept between 60 and 30 per cent of the normal prothrombin time and the dosage of dicoumarol

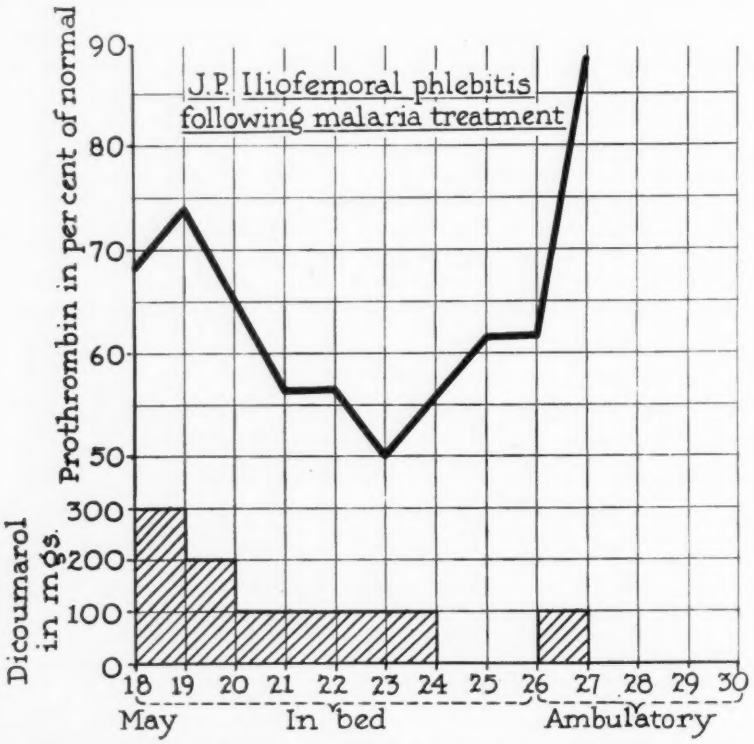

Fig. 6.—The routine treatment of iliofemoral thrombosis with anticoagulants. The administration of 5 c.c. of undiluted heparin given every four hours for the first two days is not shown in the graph. This patient arrived at the hospital two weeks after the completion of a course of fever therapy for general paresis. His history was typical of an ascending lower leg thrombosis. He received dicoumarol for six days and was made ambulatory on the eighth day, by which time the pain and edema had disappeared. One more dose of dicoumarol was given at the time when he was made ambulatory.

must be adapted to the daily determinations. Heparin is discontinued usually after two days, when the action of dicoumarol has become manifest. Dicoumarol is used until the patient is ambulatory, which may be as early as eight to ten days, unless an infarct or some other complication prevents it. In some patients with recurrent thromboses, in polycythemia with multiple thromboses, or in recurrent embolizations from the heart to the peripheral arteries, dicoumarol has been given for many months, with control of the prothrombin level once a week. When dicoumarol is suddenly stopped, a thrombosis may become manifest.

Criticism of the Method: Propagation of thrombosis or embolism has been said to have occurred during or immediately after discontinuation of the anticogulant.[19] With adequate dosage and slow tapering off with discontinuation of the drug, we have not observed such phenomena. More objectionable is the difficulty of control and the danger of hemorrhage in postoperative patients.

CASE 4.—A. G., a 56-year-old optometrist, had had fibrillations for many years. Two weeks before entrance to the hospital he suffered a cerebral embolus. Ten days later a right femoral embolus occurred which was not seen by us until three days later, when the lower leg was obviously lost. It was amputated just above the knee. Dicoumarol was promptly started with heparin. The prothrombin levels are shown in Fig. 7.

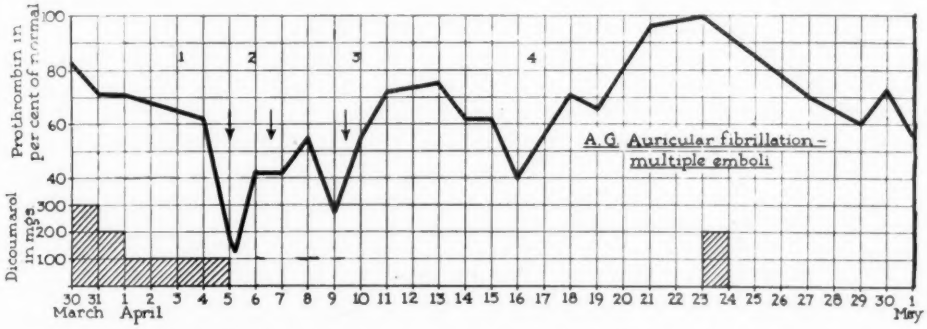

Fig. 7.—Prothrombin levels on A. G., a 56-year-old optometrist, with known fibrillations for many years, who entered St. Luke's Hospital March 29, 1944, because of a right femoral embolism suffered forty-eight hours previously. A week previous to this vascular accident he had a cerebral embolus producing considerable difficulty with speech. On examination the right lower extremity was obviously lost, but it was packed in ice with the hope of gaining some time for collateral circulation. Dicoumarol was started promptly with the customary schedule of 300, 200, and 100 mg. for the first three days. After six days of dicoumarol, the prothrombin level dropped to 17 per cent of normal and this was all the more undesirable since a gulliotine amputation of the right leg was performed under refrigeration on April 3. A huge hematoma formed in the stump. (1) Amputation; (2) 50 mg. of vitamin K given intravenously April 5 and 7 raised the prothrombin level to 53 per cent of normal, but next day it fell again to 28 per cent. Another 50 mg. of vitamin K and 500 c.c. of blood were given at (3). At (4) it was necessary to start digifolin, gr. 1½, three times a day intramuscularly. Dicoumarol had been stopped April 5, but a single dose of 200 mg. was given again, April 23. This patient was sensitive to dicoumarol, possibly because of a cardiac cirrhosis of the liver. The effect of vitamin K was temporary. The effect of digitalis may have raised the prothrombin level to a level never reached before. Owing to an error of the resident staff, and in spite of a standing order, he received no dicoumarol on April 18 and thereafter, when his prothrombin level began to rise. He died of multiple pulmonary emboli from the right heart. This graph indicates some of the difficulties encountered when dicoumarol is administered. Both vitamin K and digitalis may have increased the clotting tendency, whereas the hepatic damage made the patient sensitive to dicoumarol.

3. *Paravertebral Sympathetic Block.*—Some of the symptoms following venous thrombosis are due to a spasm in the peripheral vascular tree. This is especially evident when the iliofemoral segment is suddenly occluded and is surrounded by a periphlebitic exudate. A paravertebral block of the lumbar sympathetics will relieve the pain and much of the edema and restore the arterial pulsations, which are frequently diminished. They may even be absent and give rise to the diagnosis of arterial embolism.

A case in point is that of H. R.

CASE 5.—H. R., a 52-year-old man, entered St. Luke's Hospital Dec. 1, 1943, with an attack of nausea, vomiting, and abdominal distention.

Past History.—In July, 1942, the patient had a myocardial infarct, since which time occasional anginal pain occurred. He had been taking unknown amounts of digitalis off and on, on his own volition, until the time of entrance to the hospital.

Diagnosis of acute posterior infarct was made and emergency treatment instituted. He rapidly improved but twelve days after admission, after preliminary abdominal and left suprapubic cramping, the entire left lower extremity became cyanotic and pulseless. Pain was intense at the groin. Edema was marked only in the thigh. The adductor muscles were tender on pressure.

Diagnosis of left iliofemoral thrombosis was made with reflex arterial spasm. Papaverine, gr. 1, by mouth did not relieve the pain. Paravertebral block resulted in restoration of color and arterial pulses. The foot of the bed was elevated on a chair. Heparin-dicoumarol treatment was started. Within twenty-four hours the circumference at the ankle was reduced by one inch and at the thigh by four inches. There was no difference between the two lower extremities.

Course.—Two weeks later the swelling in the thigh recurred; a hard inguinal lymph gland became palpable. A firm cord was felt left of the prostate, which was large and tender. X-ray was given to this area. The attack subsided and he was discharged with a rubber stocking after fifty-one days in the hospital.

Follow-up.—Three months later there was considerable edema at the ankle. He had not worn the stocking consistently, but unquestionably the second, periphlebitic block at the groin contributed to his permanent edema.

Criticism of the Method: The method can be readily acquired with little practice and seems harmless. It will not protect the patient from an embolus,[20] nor can it protect him from residual edema if the extent of the thrombus is too great. Whether it would localize a plantar vein or calf muscle thrombosis by releasing venospasm proximal to the clot is not certain, but phlebograms have been reported demonstrating the release of venospasm following sympathetic block.[21]

Sympathetic block may be useful many years following an iliofemoral thrombosis. It is then capable of relieving a chronic causalgia-like pain with edema which originates in the periphlebitic reaction around the occluded vein. Stripping such a vein has been useful,[22] but one or two sympathetic blocks may be equally effective.

The following case is illustrative.

CASE 6.—G. D. S., a 54-year-old lawyer, developed cramping in the left calf following a bicycle ride in 1940. The pain and swelling ascended to the groin and to the scrotum. When seen two years later there was a diffuse swelling from midcalf to groin. Following a paravertebral block with procaine and an adequate elastic stocking, the swelling of the thigh decreased 5½ inches. Six months later use of the stocking was discontinued. All pain and edema disappeared. In 1943 he developed a sudden pain in the gluteal region and along the sciatic nerve following the injection of a hemorrhoid done elsewhere. This subsided in two weeks and there was no recurrence of swelling during the last year.

4. *Proximal Vein Ligation.*—Many authors have advocated the extraction of the clot or the proximal ligature of the vein to prevent embolism.[23] The method seems obviously indicated when, after a pulmonary infarct, the site of thrombosis is recognized in one or both calves,

when the thigh is not swollen, and the femoral vein is not tender. Much less of an indication exists when the patient is seen in a stage of fully developed iliofemoral thrombosis, which is tender, adherent, and cannot always be completely extracted by suction. In such a situation the operation seems unnecessary unless one wishes to tie the common iliac vein, a procedure still under discussion.[12]

Criticism of the Method: Many femoral veins seem to be tied unnecessarily. The visualization of the deep veins of the lower leg has been advocated for a localization of the thrombus,[24] but in my experience it results in clear-cut information only when a clinical study is equally conclusive. Its results are questionable in many instances; the drug (35 per cent diodrast) may produce thrombosis in tortuous veins with retarded flow. The edema resulting from the ligature is negligible if the femoral vein is ligated below the profunda and if the profunda remains open. Some of our first experiences with ligation of the femoral vein indicated that thrombosis of the unobstructed collaterals may follow aspiration and produce massive edema. Ligation of the common femoral vein often leaves a huge edema.

CASE 7.—A man, W. B., entered St. Francis Hospital complaining of sudden cyanosis and dyspnea of thirty hours' duration. Four weeks prior to admission his left ankle swelled and the calf became painful.

Past History.—Two years previously the patient had a prostatectomy followed by dyspnea. There was an attack of pleurisy one year ago. He was a heavy drinker.

On admission the entire left leg was warmer than the right. It was not swollen in the thigh but the Homans sign was positive. A bedside film showed increased density throughout both lungs with multiple emboli. Aug. 9, 1940, the femoral vein was exposed at the groin. The vascular sheath was edematous. The artery was separated from the vein with difficulty. The vein was thick, edematous, and distended. The origin of the profunda was visualized and a braided silk ligature was placed just distal to it. A second ligature was placed one inch below the first one. The vein was cut and both ends were transfixed. Proximal to the ligature the vein was nicked; a glass suction tip aspirated a lot of small clots until bleeding was free from above. The incision was closed with interrupted sutures. The profunda was aspirated and free blood obtained. Heparin could not be administered since it caused a severe reaction in the patient.

Convalescence was uneventful. He was out of bed and walking about, but the left saphenous vein became red and tender. A definite phlebitis developed. This resulted in a residual edema, when the patient was seen one year later. Three years later there was a permanent moderate fibrosis and enlargement of the entire leg. He has to wear a stocking continuously.

CASE 8.—E. K., a woman 47 years old, had been under medical care for the past ten years for renal glycosuria, amenorrhea, repeated ankle strain, and five attacks of calf muscle thrombosis. There were several attacks of dizziness and choking with fever in her history. The perforating veins were incompetent below the knee. June 12, 1943, the femoral vein was exposed below the profunda. It was thickened, but empty, and was transected. Four months later, this leg was more cyanotic but not any more swollen than prior to the ligature. Eleven months later an acute phlebitis developed on the side of the femoral ligation. There were hard lumps in the previously incompetent perforators in the calf. Swelling and pain were considerable.

Elastic support and one week's course with 60 gr. of sulfadiazine helped to calm the process. While this patient was now protected from emboli, the attacks of phlebitis continued. Note also that the emboli occurred from a seemingly infectious, irritative type of clot.

*Roentgen-ray Therapy:** Since animal experiments convinced us that the absorption of thrombophlebitic edema may be hastened by x-ray therapy,[25] this form of treatment has been consistently used since 1933 in selected cases. While we have no knowledge of the effect of roentgen rays on the organization of the thrombus, the effect on the periphlebitic exudate and on the concomitant lymphangiitis and lymphadenitis is unmistakable. This effect is well demonstrable in cases of superficial periphlebitis and lymphangiitis, where one or two treatments visibly and palpably decrease the red, edematous streaks of inflammatory exudate. The dosage and the timing of repeated doses are important. If, in acute phlebitis, a dose of 200 r. units is given, a serious general reaction may occur with chills, fever, and a temporary bacteriemia. Such a dose will be occasionally administered by an overzealous x-ray resident and is definitely inadvisable.

The surgeon should follow the results of roentgen therapy and not order another dose until the response to the first dose has subsided. One of us reported that a 30 to 40 per cent erythema dose of roentgen ray (125-135 r. units) with heavy filtration will produce a rise in temperature over the affected veins, which is markedly exaggerated compared with the response of a normal area.[26] If such doses are given repeatedly an exacerbation of phlebitis may result.

A surprisingly large number of patients have been seen who have gone through an active stage of deep venous thrombosis of the lower leg with or without embolization and with or without proximal ligation of the deep vein. A residual, latent infection may remain, with intermittent aching during changes in weather, slight local rises in skin temperature, and intermittent edema. A few small doses of roentgen-ray treatment are beneficial in this group, together with adequate elastic support. Case 9 is an example of this.

CASE 9.—Dr. H. D. had repeated attacks of pleurisy, until after the third one a deep thrombophlebitis in the left calf was discovered. He was treated by glycerin-gelatin casts. The thrombosis had reached the iliofemoral segment and was obviously of many months' duration. For four to five days at a time this leg would ache, swell more. There were persistently increased temperature and higher oscillometric readings over the affected limb. Three doses of roentgen-ray treatment consisting of 80 r. units with 2 mm. aluminum and ¼ mm. copper filter, given at one-week intervals, have effectively relieved the ache and some of the edema.

RESULTS OF TREATMENT

Conservative Therapy.—No figures are available since many hundreds of patients have been treated with conservative therapy. The residual

*The majority of these patients were treated by Dr. E. L. Jenkinson of St. Luke's Hospital. Thanks are also due to Dr. James B. Case, Dr. E. E. Barth, Dr. Gentz Perry, and Dr. Alfred C. Ledoux for their cooperation.

edema and the long period of disability, however, are marked, and an effort should be made for a more intensive type of therapy.

Anticoagulant Therapy.—All that can be said for the sixty-eight patients treated thus far is that not one of them developed an extension of the clot or an embolus, while they were receiving the drug.* Three patients had to have repeated courses of dicoumarol months apart since the original site of the clot became active again. One patient who had a femoral vein ligation and was kept on dicoumarol for ten days, when allowed to get up without further dicoumarol therapy, developed a thrombosis of the deep veins in the opposite leg. The superficial femoral vein was promptly tied on the second side. No edema developed. She was kept under dicoumarol for one month. Three patients are under continuous dicoumarol treatment, taking 300 mg. a week, but how long this can be kept up without any damage is not known. One of these has recurrent attacks of retinal vein thrombosis. Another, with rheumatic heart disease with multiple emboli to brain and extremities, controls her dosage with capillary coagulation times. The dosage has now been so regulated that she takes 300 mg. whenever the coagulation time returns to two minutes. A third patient takes 100 mg. five days of a week; this is far too much for the average patient, but her polycythemia makes her unusually resistant to dicoumarol.

Paravertebral Block.—We have used this paravertebral block occasionally since the report of Leriche, and more extensively since the reports of Ochsner and De Bakey.[17] If the block is done early in the painful iliofemoral type (Group 3) it may hasten convalescence and disappearance of edema. However, with papaverine, heat to the abdomen, and high (eight to ten inch) elevation of the foot of the bed, our results are not much inferior to that obtained by paravertebral sympathetic block. We now limit the use of the method to patients whose arteries are in noticeable vessel spasm, whose toes are cold and blue, and who suffer great pain. Most patients, however, exhibit warm toes, large oscillations, and other evidence of inflammatory hyperemia. The results of paravertebral block in the late edemas, with neuritic pains aggravated by weather changes, are often striking. One or two injections combined with elastic support have relieved patients from long-drawn-out discomfort. Seventy-eight patients in a group have been injected for thrombophlebitis, but the method is used far less frequently than formerly.

Ligation of the Femoral Vein.—After trying this method in different types and different stages of thrombosis, the following indications have crystallized in our hands. (1) When the patient has had an infaret, wholly unexpected, the source of it is carefully investigated. If

*This statement requires modification since we have started the use of vitamin K to restore excessively low prothrombin levels. In two patients who showed unusual sensitivity to dicoumarol in that their prothrombin level quickly dropped to below 30 per cent of normal, the intravenous administration of vitamin K in 50 mg. doses resulted in a new vascular accident, which seemed to coincide with the administration of the vitamin. Further observations are obviously needed.

it is found to be in the calf muscles of the leg, the femoral vein is promptly tied below the profunda. (2) When the patient develops a recognizable calf muscle thrombus, which has been present for less than one week and the patient is immobilized for some other reason, the femoral vein is tied. Often a floating thrombus will be found in the common femoral vein.[12, 20]

When, however, the patient is seen with a tender, swollen thigh or groin, the clot is not aspirated nor is the vein ligated above the profunda. Also, if the thrombus is below the knee but the patient has been ambulatory for more than one week without any extension to the thigh, the vein is not tied.

A total of thirty-nine femoral vein ligations have been done since 1940.* Some of these in the light of our present experience were entirely unnecessary. One of the greatest difficulties is the estimation of the age of the clot at the level of exposure. The clot is usually much older than one imagines. When it firmly adheres to the wall its aspiration from the proximal segment is difficult and leaves mural thrombi; furthermore, it has lost its embolizing property. When the clot is recent, friable, and nonadherent, its presence is not manifested by pain or edema in the thigh. We agree with Bauer[20] that these are the most dangerous clots and the ones that need ligature.

TABLE II

DIVISION OF THE FEMORAL VEIN
(1940 TO 1944)

SITE OF DIVISION	NUMBER OF CASES	RECURRENT PHLEBITIS	PERMANENT EDEMA
Superficial femoral	15	2	2
Common femoral	10		10

All patients received anticoagulants in the immediate postoperative period. There was no pulmonary embolism. All patients wore elastic hose to the groin on discharge.

Ligation of the femoral vein above the profunda invariably results in considerable edema (Table II). We have not tried the ligature of the common iliac, but this should result in less circulatory embarrassment than when the common femoral is tied.[12] Nor has the vena cava been ligated in this series.†

The attitude of our group toward phlebograms has always been rather pessimistic. The information derived is often not in keeping with its hazards and inconveniences. We do use it if a topical diagnosis of venous occlusion is not possible. Circulation times from ankle to tongue are helpful.

*Twenty-five patients were re-examined from six months to three years after operation.

†Since this article was submitted for publication, the important contribution of Homans has appeared on the ligation of the common iliac vein or the vena cava for the bland ascending thrombosis. It is our feeling that the floating, nonobstructive clot at the iliofemoral segment is very difficult to diagnose preoperatively from an obstructive clot with well-established collaterals. Anticoagulant therapy has been our method of choice in such cases. Recently two ligations of the common iliac vein were done by Dr. J. T. Reynolds at St. Luke's Hospital.

X-ray Treatment.—This type of treatment was given a trial in superficial phlebitis of varicose veins, in the iliofemoral thromboses with lymphadenopathy, in the migrating type of superficial phlebitis, and in the chronic latent deep phlebitis with exacerbations. The treatment is obviously directed against the periphlebitic infiltration and exudation. Naturally it will be least effective in the type of lesion which is activated by reinfection or allergic processes. In the migrating type of phlebitis seen in Buerger's disease, the response has not been satisfactory. The total number of cases on record is 74. Of these the diagnosis was varicose phlebitis in 35, migrating phlebitis in 10, iliofemoral thrombophlebitis in 26, and chronic latent phlebitis of the lower leg in 3 patients. Many of these cases would be treated today by a short intensive therapy with sulfanilamide. Penicillin in moderate doses, 15,000 units intramuscularly every four hours for five days, has given surprising results in three cases of migratory phlebitis; this type of treatment, however, has only been started and further experience is necessary to estimate its value.

PULMONARY EMBOLISM

Again there is no need to discuss in detail the classical picture of the massive pulmonary embolus, which obstructs the main artery or its two branches simultaneously and which kills the patient in less than ten minutes. But as pointed out previously, only 8.3 per cent of patients die in less than ten minutes, and 33 per cent die in less than one hour. Approximately 60 per cent of the patients with fatal emboli live from one hour to several days.[27] These figures only refer to the fatal emboli, but it is sufficiently known that only about one-fifth to one-fourth of these emboli are fatal at the first insult.[11]

TABLE III

PULMONARY EMBOLISM

RECOGNITION
Sudden onset of shock with rapid weak pulse, restlessness, difficult, rapid breathing, sweating and pallor, pain in chest, fainting, collapse, or unconsciousness. Apt to be in a patient who has phlebitis, is convalescing from an operation or delivery, or is a known cardiac.
EMERGENCY TREATMENT
By Nurse
1. Place in semisitting position.
2. Start oxygen by catheter or mask immediately. Tanks are on each floor.
3. Give 1/75 gr. atropine sulfate, hypodermically, immediately.
4. Call intern.
By Intern
1. Give a second dose of 1/60 to 1/75 gr. atropine sulfate intravenously (if previous injection of atropine has not caused flushing of face and dilation of pupil).
2. In any case give ½ gr. papaverine hydrochloride intravenously.
3. Repeat atropine and papaverine three or four times a day.
4. Order portable chest film and electrocardiogram.
Note
Morphine, adrenalin, or digitalis may aggravate the condition.

This treatment is useful even if patient is suffering from some other condition such as coronary occlusion or a cerebral vascular accident.

These figures mean that there is sufficient time to treat the majority of these patients, first of all for the episode itself, and second for the prevention of a second or third infarct which might become increasingly dangerous. The recognition of the early signs and symptoms has been stressed to the nursing staff. A small set of instructions is posted on each floor, since it has been our experience that in large hospitals much important time is lost until the intern arrives (Table III).

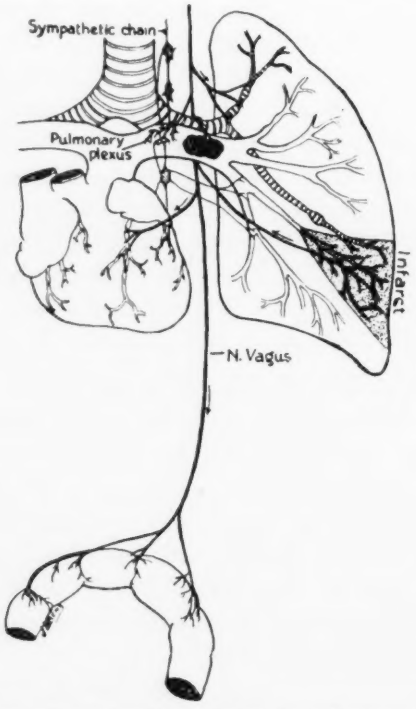

Fig. 8.—The radiation of autonomic reflexes in pulmonary embolism. The afferent impulses travel mainly in the vagus and radiate back to the lung as bronchoconstrictor and bronchosecretory fibers. They produce vagal inhibition of the heart and depress blood pressure. They can cause pylorospasm and intestinal colics, producing severe abdominal pain. (From SURGERY 6:339, 1939.)

The rationale of this emergency treatment is based on the assumption that embolism kills not only because of asphyxia, failure of the right heart, or insufficient venous return to the left heart. True enough, these conditions prevail when the main pulmonary artery or both right and left branches are simultaneously obstructed. However, we have shown post-mortem records to indicate that patients may die from a small embolus obstructing an insignificant area of the lung.[27] But also, on the basis of animal experiments, we have concluded that a widespread radiation of autonomic reflexes occurs during embolism, which affects the heart, the pulmonary vascular tree, the bronchi, and the gastrointestinal tract[28] (Fig. 8). These reflexes are predominantly vagal and produce spasm of smooth muscle; thus the use of atropine and papaverine seems indicated. Morphine and digitalis both sensitize the vagus and may thus facilitate such reflexes. Epinephrine, frequently employed in acute

hypotension, may lead to pulmonary edema in the presence of an increased pressure in the pulmonary artery which exists in cases of pulmonary embolism. These drugs have been tried in the animal experiment and have been shown to have deleterious action.

These emergency measures have been in use at St. Luke's Hospital for over four years. Of the forty-five patients on whom we have adequate records, thirty-five were relieved of their symptoms and did not die of that attack. Ten patients died with six autopsies. These autopsies showed massive arterial obstructions with coils of clots in the right ventricle; obviously this type of treatment could not help.

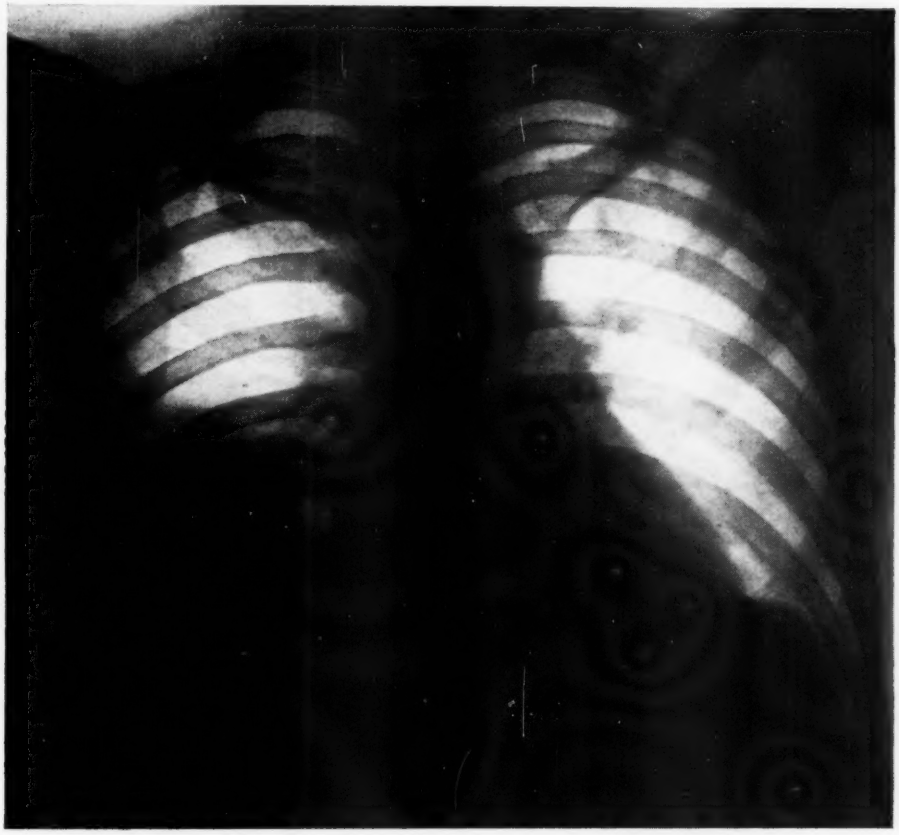

Fig. 9.—Pleural effusion following typical pulmonary embolism followed by iliofemoral thrombosis. The embolus occurred ten days after cholecystectomy. The left foot and lower leg were slightly warmer. Repeated pleuritic effusions are not infrequently seen, being due to multiple emboli.

Attention should be called to the syndrome of the slowly fatal pulmonary embolism, when death finally occurs from right heart failure many hours or several days after the initial attack. If pulmonary embolectomy is to be done at all, in such a case a trial would be worth while, as Pilcher suggested.[29]

The x-ray diagnosis of pulmonary emboli is very disappointing. The wedge-shaped infaret is the great exception.[30] It should be remembered

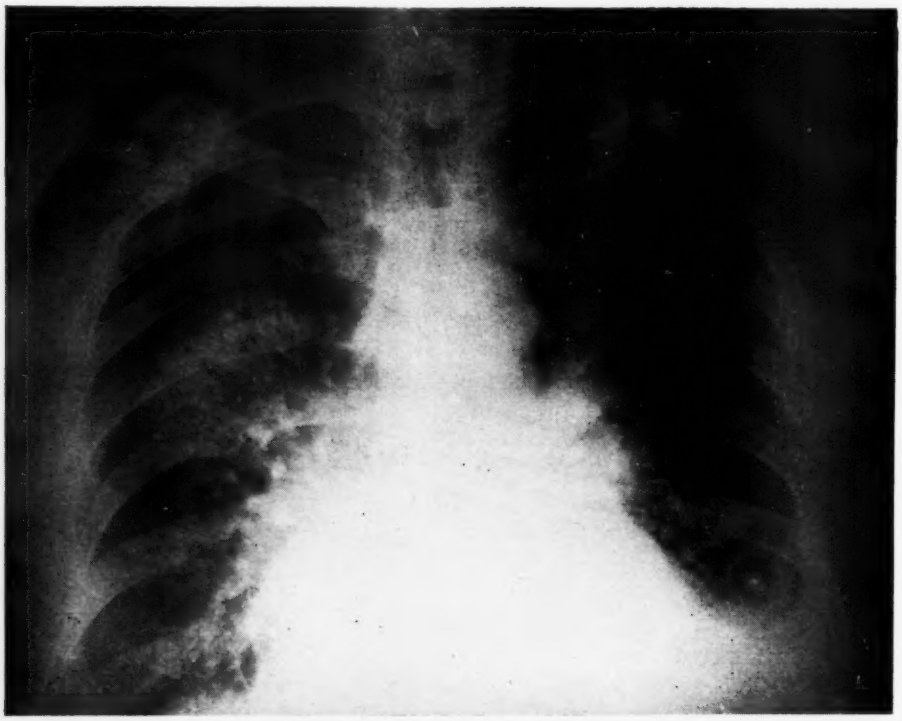

Fig. 10.—Multiple pulmonary emboli following a punch prostatectomy, verified by autopsy. This patient was suspected of having multiple pulmonary metastases of carcinoma when he suddenly died from an embolus.

Fig. 11.—Atelectasis of the left lower lobe ten days after a hernia operation. In a previous communication[2d] we stressed the mechanism of reflex pulmonary atelectasis following emboli or chest trauma.

that not all emboli produce hemorrhagic infarcts; anemic areas may be translucent; areas of atelectasis or emphysema may be visible, depending on the extent of bronchial obstruction. Pleuritic effusions (Fig. 9), embolic atelectases (Fig. 10), and embolic pneumonias (Fig. 11) may so mask the origin of the lesion that the source of the embolus is not looked for. Following the survival of the first embolic episode the primary source ought to be eliminated if possible. In case of a thrombus in the plantar or calf muscle veins, the ligation of the superficial femoral vein seems indicated. We are unconvinced, as stated previously, that the aspiration of the common femoral vein, in the presence of an iliofemoral thrombus, is necessary. If the clot had been really loose it would not be there any more; if it is organizing, the operation is unnecessary; the clot may reform after a complete cleaning out of the iliofemoral segment if anticoagulant therapy is inadequate.

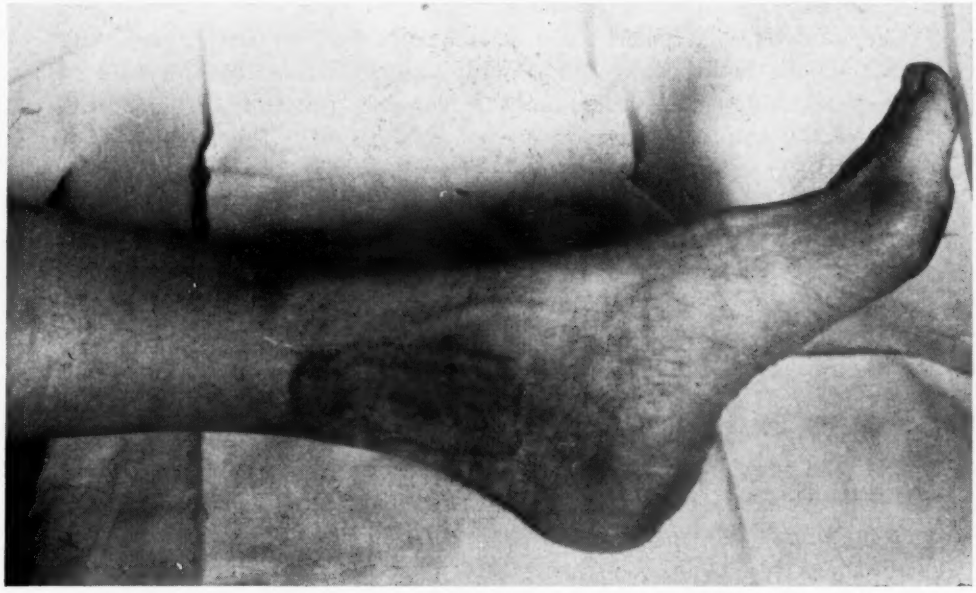

Fig. 12.—Dermatone graft on a chronic recurrent thrombophlebitic ulcer. Note the small area of necrosis in the center of the graft, which came on two years after grafting. After two gelatin-glycerin casts the small defect readily healed.

If the primary source is in the pelvis or the right side of the heart, only anticoagulants can be of any use. These may increase hemoptysis or the pleural effusion but not to an alarming degree. In thirty-one patients receiving adequate heparin-dicoumarol therapy* in the presence of an infarcted lung, there has been no detectable increase in the size of the infarct.

On the contrary, we believe we have recognized, in conjunction with our medical consultant, Dr. G. K. Fenn, cases of pulmonary infarction

*By adequate therapy we mean the establishment of a prothrombin level between 30 and 60 per cent of normal, which is jealously guarded from getting higher or lower.

where the pulmonary embolus had grown proximally by a superimposed thrombosis, giving rise to increase in dyspnea, in chest pain, and in the area of dullness. This propagating thrombosis[31] is an added indication for anticoagulant therapy.

DISCUSSION

The problems arising in cases of thrombo-embolism are many and controversial. A clarification of these questions can be expected when all those interested in these problems accept a uniform nomenclature. The syndromes of plantar vein, calf muscle, iliofemoral, and pelvic thrombosis are clearly defined, although they may merge into each other. The age of the thrombus ought to receive consideration since there can be no point in curetting out some old white granulation tissue from a well-obliterated, well-organized thrombus; nor is a hasty bilateral ligation of the femoral vein below the profunda going to benefit the patient with a pelvic or right auricular thrombus.

The study of the patient's clotting mechanism by the heparin tolerance or the modified prothrombin times permitting the detection of hyperprothrombinemia seems to us a valuable procedure since it determines the activity of the thrombosis and signifies the possibility of additional thrombotic or embolic phenomena. The test might also be applied to pick out surgical patients who are apt to develop thromboses and who then can have prophylactic anticoagulant therapy. Such a study is now under way but will evidently require a great deal of material to be of any statistical value.

The selection of different methods of therapy in different stages of the disease naturally varies in different clinics. We are much impressed with the value of anticoagulants throughout the therapy and prophylaxis of pulmonary embolism but admit that in their present form they are not simple enough to have a wide distribution. It is our feeling that the control of the clotting mechanism throughout the hospital stay of the patient might well be placed in the hands of the medical department, just as are the insulin requirements of a surgical diabetic patient. We have been impressed with the clear-cut results of superficial femoral vein ligation in the case of thrombosis of the lower leg. But a large number of patients, especially in the nonhospitalized group, are seen with a fully developed iliofemoral thrombus of some days' duration. Just what the limit of operability is in these cases is ill defined, but we ourselves have been guilty of exposing and aspirating well-organized thrombi, which is obviously unnecessary.

The use of paravertebral sympathetic block has been limited to patients exhibiting definite vasospasm with cold, pale extremities and diffuse ache, in which cases its effect is truly remarkable. These cases, however, are not numerous.

While the danger of embolism has aroused the interest of many workers, the problem of residual edema and induration requires equal con-

sideration. It was pointed out in 1931[15] that thrombophlebitic edema is rich in protein, that it is easy to mobilize at first, but that the clotted plasma and the resulting fibroplastic reaction produce irreversible damage. The management of the late thrombophlebitic indurations and ulcerations is a problem in itself. Such lesions produce great loss of time from work, much suffering. A radical excision of the late thrombophlebitic ulcers covered with split-thickness grafts has been very useful, but unless the edema can be kept under fair control, the graft may break down again (Fig. 12). Of twenty-three split-thickness grafts which had a primary 85 to 100 per cent take and were firmly healed on discharge, six broke down again at the end of one year, in spite of adequate elastic support. Small perforating veins develop and thrombose under the graft, and over them the skin breaks.

Every effort should be made, then, to hold the edema down to the minimum. Increasing edema may develop from excessive standing and bouts of hot weather, and often from a reactivated ringworm infection which may act either by adding a slight lymphedema to the preexisting lesion or by producing sensitization phenomena similar to those seen in Buerger's disease.

SUMMARY

The incidence of venous thromboses in peripheral veins is much higher than ordinarily suspected. Four groups of venous thromboses, namely, the superficial venous thrombosis, the ascending plantar vein thrombosis, the calf muscle thrombosis, and the pelvic vein thrombosis, can be recognized as being the primary sources of clotting. Any one of these may produce, by propagation, an iliofemoral thrombosis, the classic milk leg. The treatment of such thromboses should vary according to the primary site, the extent and the age of the thrombosis. Anticoagulant therapy, paravertebral sympathetic block, proximal venous ligation, and roentgen-ray therapy all have their indications but should be used selectively. Visualization of the venous system by opaque substances may be used occasionally but its routine use does not seem necessary. Pulmonary embolism is still often the earliest manifestation of an unrecognized thrombus in the periphery; its appearance calls for emergency measures and, following the recovery of the patient, for a thorough investigation of the source of the embolus, since recurrent emboli are increasingly dangerous. Early attention must be paid to the elimination of clotted plasma from the thrombophlebitic leg, since much permanent disability may result from this source.

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ETIOLOGY AND PREVENTION OF THROMBOSIS OF THE DEEP LEG VEINS

A Study of 400 Cases

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THE problem of venous thrombosis and its most serious complication, pulmonary embolism, rightly commands the continued interest of all physicians.

Although incorporated in the wealth of publications of past years, certain fundamental and now well-authenticated facts concerning venous thrombosis and embolism are much in need of reiteration and emphasis. Textbooks in all of the specialties of medicine have almost universally chosen to repeat shopworn phrases, many of which are no longer in keeping with newer and well-documented information. For example, all venous thrombosis is still commonly referred to as "thrombophlebitis." Yet, as Ochsner and DeBakey[1] have pointed out, the rational consideration of the mechanism and prognosis of venous intravascular clotting demands that it be divided into two types: (1) phlebothrombosis, defined as venous occlusion unassociated with inflammation, the clot being loosely attached to the vein wall and (2) thrombophlebitis, clotting associated with and dependent upon inflammation of the vein wall, with the result that such clots are usually firmly attached. We fully agree that such a distinction is basic and fundamental. There is, moreover, a woeful lack of appreciation as to which veins serve as the commonest sources of thrombotic emboli—a vital feature of the problem from the point of view of prevention and treatment. It is still generally assumed that pulmonary emboli usually arise from clots in the femoral or the pelvic veins or from the right side of the heart, disregarding the now ample data to the contrary. Still another long and fondly held fallacy is that only the surgical patient is in danger of sustaining a pulmonary embolus. Again published figures are disregarded, for it is a fact that patients suffering from medical diseases are fully as susceptible and just as frequently die from pulmonary embolism. Finally, there has been great neglect of the adage that "an ounce of prevention is worth a pound of cure" with respect to phlebothrombosis and pulmonary embolism. The literature has been, and still is, cluttered by papers dealing with methods of diagnosis, refinements and

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modifications of these procedures, and suggested means of treatment, all assuming that willy-nilly, thrombosis will take place and that "closing the barn door after the horse is out" is the desirable thing. It is true that some writers mention possible means of preventing thrombosis but unfortunately they propose methods not easily carried out, or bury the paragraph on prevention so deeply and inconspicuously in a maze of discussion that the casual or inexperienced reader fails to grasp its significance.

After several years of experience it has become our conviction that the only real hope of lessening the toll of deaths from pulmonary embolism lies in the widespread acceptance of the newer and well-proved facts as to the causes, the nature, and the anatomic location of most instances of venous thrombosis. Progress cannot and will not be made until this is accomplished.

REVIEW OF PERTINENT LITERATURE

Lack of recognition that the deep veins of the leg are the most frequent site of thrombosis and the most prolific source of both fatal and nonfatal pulmonary embolism long remained unknown for two reasons: (1) symptoms referable to such thromboses are likely to be absent or so slight that they are overlooked clinically and (2) restrictions upon necropsy dissection of the extremities.

Frykholm[2] credits Denecke,[3] 1929, and Olow,[4] 1930, with proving that the earliest clinical symptoms of thrombosis of the lower extremities appear in the sole of the foot and in the calf, suggesting that these are the initial seats of clot formation. As early as 1934, Homans[5] in this country, supported by clinical and pathologico-anatomic observations, emphasized the great importance of the veins of the calf as areas of origin of ascending thrombi.

Very possibly because of lesser restrictions on the extent of dissections, the first extensive examinations of leg veins were done in Germany. Thus, Rössle[6] in 1937 published observations based on 324 postmortems in persons over 20 years of age. Of these, 88 (27.1 per cent) harbored thrombi in the veins of the calf. Concomitant thrombosis of the femoral vein was found 38 times. In only 7 instances did Rössle find thrombosis of the femoral or hypogastric veins in the absence of thrombosed leg veins. It was his opinion that although emboli originating from the leg veins are rarely fatal, they are nevertheless significant because it is from thrombi here, propagating into the femoral veins, that massive emboli spring. Even so, in carefully dissected preparations he discovered 3 instances of pulmonary embolism accountable for only on the basis of an origin from the calf veins.

Equally interesting is Neumann's[7] report on a series of 165 consecutive autopsies in which the venous system was widely and thoroughly searched for thrombi, with particular attention to the veins of the lower

extremities. In the 100 subjects exhibiting thrombosis of the legs, the localization was: plantar region, 71 per cent; internal malleolar region, 17 per cent; leg, 87 per cent; thigh, 22 per cent. The calf veins were much more often affected alone (29 per cent) than were the plantar veins alone (12 per cent). Neumann postulated two clinical types of thrombosis, based on the site of origin: (1) a benign variety, starting in the veins of the legs and characterized by slow progression of the clots, increasing in frequency with age and having a tendency toward multiple but nonfatal emboli; and (2) a malignant form, centered in the plantar region and typified by rapidly progressing thrombosis, occurring in younger people, not rising in frequency with age and tending toward fulminating, fatal embolism of the lungs. He expressed the belief that the source for both types is a thrombus that has progressed into the veins of the thigh. Of his subjects with thrombosis of the lower extremities, 11.8 per cent had fulminating fatal pulmonary embolism, and of these more than 80 per cent had clots in the veins of the feet and calves. If one includes the cases of nonfatal multiple emboli, the lower extremities account for 52.8 per cent of the clots lodging in the lungs.

Putzer[8] investigated 370 bodies for thrombi in the lower leg and observed calf vein involvement in 100 of these (27 per cent). The right side was affected slightly more often than the left, but in nearly all instances the process was bilateral. There were 47 men and 53 women, 86 per cent of whom were between 40 and 80 years of age. All but three were classified as medical rather than surgical.

A very thorough study of thrombosis of the pelvic and leg veins was published by Frykholm[2] in 1940. The following list gives the locations and number of instances in which he found clots: iliac, 2; hypogastric, 3; visceral pelvic, 5; femoral (above profunda), 4; deep femoral, 9; adductor muscle, 16; femoral (below profunda), 5; popliteal, 23; calf muscle, 39; anterior tibial, 0; posterior tibial and peroneal, 25; malleolar and plantar, 2. With negative results he also searched the veins of the gluteal region and the extensor musculature of the thigh. There were 24 examples of pulmonary embolism but Frykholm fails to state which of the many sources he believed to be responsible for the embolus. Always, he observed, progression of the thrombotic process was in the direction of normal venous flow.

Two of us (W. C. H. and V. D. S.), with the collaboration of Robertson and Snyder,[9] routinely removed the calf muscles in an unselected group of 351 autopsies. Later we had the opportunity of testing the validity of our conviction that the most important etiologic factor in phlebothrombosis of the lower extremities is simply confinement to bed for any reason whatsoever for more than a brief period. In order to obtain adequate control clinically, this study was limited to one hospital (Multnomah County) and was continued until the total number of again unselected autopsies reached 200, the same number investigated

the first time.[9] Our second study was extended to include dissection of the femoral veins and those of the adductor muscles, shown by Frykholm[2] to be almost as frequently occluded as the major veins. We are now in a position to compare results with previous investigators, save for the plantar veins.

On the basis of the findings in the 351 cases, published in 1941,[9] we came to the following conclusions:

1. Thrombosis of the deep veins of the leg is appallingly frequent among middle-aged and older persons forced to bed for varying periods of time, the incidence of thrombosis being 52.7 per cent.

2. Bilateral involvement was found 110 times and unilateral, 75 times. The right side alone was affected a little more often than was the left. Thrombi formed in the veins accompanying the larger arteries far more frequently than in other veins and were present in the soleus muscle more often than in the gastrocnemius.

3. Fatal pulmonary embolism was responsible for 3.13 per cent of all deaths; in 45.4 per cent of the cases of death from such embolism the most probable source was thrombosed leg veins. There is good authority for the belief that although fulminating emboli often spring from the femoral vessels, thrombosis here represents an extension from older clots in the legs and feet. From the standpoint of prophylaxis and treatment, recognition of this is most important.

4. Lesser emboli frequently originate from the veins of the calf. Showers of these, even though of small diameter, may consist of long clots, which, by buckling or coiling, are capable of occluding even the major pulmonary arteries. Repeated embolic episodes are more frequent than a single massive attack. Multiple small fragments can also do harm, by placing an added burden on an already embarrassed circulatory system.

5. In this series there was little difference in the incidence of thrombosis between medical (53.2 per cent) and surgical (46.9 per cent) patients or between men (52.2 per cent) and women (53.5 per cent).

6. Phlebitis, either as a cause or as a complication of thrombosis, had a minor role in our cases (8.1 per cent).

7. As a rule, phlebothrombosis of the deep veins of the leg is clinically silent and for this reason is likely to be forgotten until embolic phenomena appear.

8. We are of the opinion that the greatest single factor favoring thrombus formation in the lower extremity is sudden confinement to bed of a previously ambulatory older person without the benefit of exercise or the aid of gravity in the maintenance of an efficient venous circulation.

9. Planned and supervised voluntary movement and the elimination of too much comfort for the legs should do much to reduce the incidence of thrombosis and its all too frequent sequel, pulmonary embolism.

PRESENT STUDY

As previously stated, our purposes were: (1) to compare two series of equal size from the same hospital, (2) to determine the incidence of thrombosis of the femoral and adductor veins, and (3) to learn, if possible, the effects of exercise on thrombus formation.

At the outset it was recognized that the number of individuals who could safely be exercised might be limited. Previous experience[9] had shown that on occasion phlebothrombosis may occur within two days after beginning recumbency. For this reason, in order to be perfectly safe, all persons not known to have been ambulatory as recently as forty-eight hours before admission were excluded. Then, too, as is common in charity institutions, many suffered from senility, debility, serious cardiac disease, and other states, so that they could not or would not move voluntarily, and this, along with a shortage of nurses, made it impractical to attempt to institute passive movement or massage. So that our efforts would not be too disseminated, it was decided to concentrate on one department, medicine, leaving to individual wishes and initiative whether exercise would be ordered in other departments. Thus, the number of suitable subjects was certain to be small.

Listed here are the post-mortem findings in the 169 instances that proved suitable for comparison of the possible effects of exercise, or the lack of it.

Group I

In hospital forty-eight hours or over (exercised, or ambulatory up to forty-eight hours before death)

Without leg vein thrombosis		
Medical service	27	
Surgical service	5	32
With thrombosis of leg veins		
Medical service	5	
Surgical service	2	7
Total		39
Per cent exhibiting thrombosis		17.9

Group II

In hospital forty-eight or more hours (not exercised) and nonambulatory before death

Without leg vein thrombosis		
Medical service	46	
Surgical service	15	61
With thrombosis of leg veins		
Medical service	42	
Surgical service	27	69
Total		130
Per cent of nonexercised, nonambulatory patients with thrombosis		53.07

Exact comparison is, of course, impossible owing to the inequality of numbers in the two groups. Unfortunately too, the number of exercised persons is small, but, in so far as it is permissible to make any statements, the incidence of phlebothrombosis is 35.17 per cent less among those who were exercised.

All pertinent figures and percentages gleaned from the two studies have been listed in parallel columns in Table I.

TABLE I

COMPARATIVE DATA OF CERTAIN VASCULAR PATHOLOGY, SEX, AGE, AND SERVICE CLASSIFICATION OF TWO SERIES OF 200 AUTOPSIES EACH, PERFORMED AT MULTNOMAH COUNTY HOSPITAL

	FIRST	SECOND
Number of necropsies in series	200	200
Number having leg or thigh vein thrombosis	118	88
Per cent with phlebothrombosis	59	44
Number of instances with thrombosis of thigh veins	Not exam.	31
Per cent occurrence of thigh vein thrombosis	Not exam.	15.5
Number of patients with thrombi only in thigh veins*	Not exam.	3
Number of patients with combined leg and thigh vein thrombosis	Not exam.	28
Per cent occurrence of combined thrombosis	Not exam.	89.1
Fatal pulmonary embolism	7	11
Origin from veins of legs alone	4	9
From other than veins of lower extremities	3	2
Per cent of deaths from pulmonary embolism (200 cases)	3.5	5.5
Per cent of deaths from pulmonary embolism (phlebothrombosis series)	5.09	12.5
Instances of nonfatal pulmonary embolism	24	28
Total number of patients with pulmonary emboli (fatal and nonfatal)	31	39
Per cent incidence of pulmonary embolism (fatal and nonfatal)	15.5	19.5
Per cent of nonfatal pulmonary emboli (phlebothrombosis group)	20.3	31.8
Sites of origin of nonfatal pulmonary emboli:		
Leg veins alone		10
Either leg veins or elsewhere		9
Probably from other than leg veins		2
Positively not from leg veins		7
Percentage of phlebitis observed histologically	5.9	2.5
Sex classification (entire group)		
Men	131	136
Women	69	64
Age grouping (whole series)		
Youngest	16	15
Oldest	94	91
Average age	60.8	62.8
Service classification (total cases)		
Surgical	29	58
Medical	159	135
Mixed (two or more services)	12	7
Surgical patients with phlebothrombosis	16	34
Percentage	55.2	58.6
Medical cases with phlebothrombosis	95	51
Percentage	59.7	37.7
Mixed group with phlebothrombosis	7	3
Percentage	58.3	42.6

*One occurred in a patient three times hospitalized and in whom the femoral thrombus was fully canalized. The other two were located in the veins of the adductor muscle, not in the femoral vein.

It seems possible that the over-all reduction in the number of instances of leg vein thrombosis, from 59 per cent to 44 per cent (15 per cent), when carried out by the same workers, under like conditions and with identical criteria for the diagnosis of thrombosis, is ascribable to the prophylactic measures instituted at the start of the second series. In the first group 59.7 per cent of the medical patients had phlebothrombosis of the calf, while in the second study it was 37.7 per cent, a drop of 20 per cent. By way of comparison, 55.2 per cent of the surgical patients the first time showed leg vein thrombi, increasing to 58.6 per cent in the later group. In fairness it must be said that the total number of surgical cases was exactly twice that of the first study.

Death from pulmonary embolism in the new series totals 11, or an increase of 4. Taking these figures alone and without explanation, it would appear that the preventive measures failed to accomplish the desired end. Of the 11, there were 5 from the medical service and the rest from the surgical division. All, irrespective of service classification, suffered from conditions which themselves precluded exercises, or had entered the hospital after previously having been in bed too long to make it safe to move their legs. All of the medical patients suffered from congestive heart failure. Pulmonary embolism could have been prevented in these people only by prophylactic femoral vein ligation.

Of interest and of practical importance is that thrombosis of the thigh veins, particularly the femoral, seldom occurs except in conjunction with involvement of the deep calf veins. In our material there was one instance of fully healed thrombosis of a femoral vein in a man who had been hospitalized on three previous occasions, and two examples of thrombosis of small veins in the adductor muscles, neither of which extended into the femoral vein. Our observations are in keeping with those of Frykholm,[2] Rössle,[6] Neumann,[7] and Putzer.[8]

Once more we have demonstrated to our satisfaction that both fatal and nonfatal pulmonary emboli more often originate from clots in the calf veins or propagations therefrom than from any other veins. Nine of the 11 fatal embolisms arose from the legs. Ten of the 28 nonfatal emboli certainly came from the legs and 9 others may have, although other sources were possible.

Phlebitis, which we accept as an entity only in the presence of acceptable histologic evidence of inflammation, was even less frequent (2.5 per cent) than before (5.9 per cent), and we find it more difficult than ever to believe that it has anything much to do with causing or influencing the outcome of deep leg vein thrombosis.

The location of the thrombi according to muscles, or to unilateral or bilateral involvement, has not been charted because the differences between the two series are trivial. As in the first study, we can say that when thrombosis occurs in the legs it is likely to be bilateral and that clots will be found in and along the soleus muscle much more frequently than in the gastrocnemius.

Table II indicates the locations of venous thrombi in situations other than the lower extremity.

TABLE II

LIST OF VENOUS THROMBI FOUND EITHER ALONE OR IN CONJUNCTION WITH THROMBI IN THE DEEP LEG VEINS

Pelvic (broad ligament, periprostatic, periurethral)	42
Pelvic veins and/or right heart chambers	6
Right atrial appendage	2
Right ventricle	2
Renal vein	1
Hemorrhoidal veins	1
Total	54
Number of patients with both leg and other veins thrombosed	33
Number of patients without leg vein thrombosis but clots elsewhere	21
Per cent with pulmonary emboli (7 cases)	33

The extremes of age, as well as the average age of the two groups, are not significantly changed. The average age for the first group is 60.8 years and for the second, 62.8 years.

CLINICAL DIAGNOSIS OF PHLEBOTHROMBOSIS

Always there will be patients who have been in bed for more than two days before calling a physician; others will suffer from illness or trauma that make prophylactic measures impossible or inadvisable, just as in our 11 cases of fatal pulmonary embolism. It is these groups to which diagnostic and therapeutic measures should be directed. They, and any adult who must go to bed, are in real danger of phlebothrombosis and pulmonary embolism. The literature is replete with papers concerned with the signs and symptoms, the diagnostic methods, and the means of treatment of phlebothrombosis, and the interested reader will have no difficulty in finding them. It is not within the scope of this paper to discuss these features. Rather, we wish to set forth proof of the frequent occurrence of deep leg vein thrombosis, to emphasize that here is the commonest of all sources for pulmonary emboli, and to reiterate our belief that while there is a place for diagnosis and treatment of phlebothrombosis, prevention is what should ever be uppermost in the mind of the attending physician.

PREVENTION OF VENOUS THROMBOSIS

Efficient return of blood from the deep veins of the extremities is dependent upon five factors, namely: (1) the circulation time, directly related to the effectiveness of the heart, (2) the compressive action of muscular contraction on veins, (3) absence or elimination of mechanical obstruction, (4) maintenance of normal negative pressure within the abdomen and thorax, and (5) gravity. The first of these needs no discussion.

The relation of circulation time to exercise has been well shown by Smith and Allen.[10] In a study of 86 persons it soon became apparent

that the most important influence on the time of blood circulation was the temperature of the skin of the extremities. The speed of flow was decreased when the skin here was cool, and accentuated when it was warm, irrespective of whether vasodilatation was reflexly produced by heat, direct application of heat, ingestion of alcohol, or sympathectomy. Two minutes of rapid active movement of a leg lying in the supine position invariably increased the speed of blood flow; elevation to a 30 degree angle of the extremities of supine subjects always increased circulation time, as did sympathectomy.

Following a study of about 500 patients given postoperative exercises and among whom, incidentally, there were no instances of venous thrombosis or pulmonary embolism, Potts and Smith[11] sought to substantiate their belief that simultaneous deep breaths and active leg exercises at regular intervals would vary the blood flow, not only in the legs, but also the pelvic venous cistern, and thus prevent stasis and thrombosis. Variations in the volume flow of blood in the inferior vena cava measured with a venturimeter, employing the Venturi principle of producing partial constriction of a stiff rubber tube connected with the cut ends of the inferior vena cava, were studied in 6 dogs. The results were identical in all. Simultaneous elevation of both hind legs produced an increase varying from 100 to 150 per cent in the volume flow of blood in the inferior vena cava. In lightly anesthetized animals, contraction of the muscles of the hind legs occurring coincident with their elevation produced an increase of more than 250 per cent in volume flow, abrupt in onset and returning to normal in 10 to 15 seconds. Accuracy of the observations was checked by isolation and ligation of both femoral veins, whereupon elevation of the legs produced practically no change in blood flow; release of the clamps was followed by a prompt rise. Normal respiration had little demonstrable effect on blood flow; deep respiration, produced by carbon dioxide, caused irregular changes. To test the validity of the observation of Luckhardt, Alpert, and Smith[12] that the reflex inhibition of respiration will temporarily obstruct the return flow of blood to the heart, Potts and Smith[11] simulated this condition by overinflating the dog's lungs. Blood flow from the inferior vena cava dropped to almost zero, but when the obstruction in the pulmonary bed was released, there followed a prompt and marked rise in blood flow. Simultaneous elevation of the hind legs, with deflation of the lungs, resulted in an enormous increase in blood flow.

Thus is afforded experimental evidence of the efficacy of exercise, of gravity, and of obstruction upon normal venous return.

An interesting medical sidelight of the bombing of London in 1940 has a bearing upon the factor of mechanical obstruction to the veins of the lower extremities. In a short paper, Simpson[13] comments on the striking increase in the number of deaths from pulmonary embolism among elderly people who were solicitously cared for night after night in the shelters by allowing them to sit in a deck, or similar type, chair.

The wooden crossbar of these chairs caused pressure on the back of the thigh or on the popliteal vessels and the legs were dependent. Comparing the deaths from other common cardiovascular accidents such as coronary thrombosis and cerebral hemorrhage, in which there was no significant increase over the previous year, it developed that 24 persons had died from pulmonary embolism in 1940, in contrast to 4 in 1939. Many of these people first consulted their physician on account of swollen legs and the condition became known as "shelter leg."

None of the five factors mentioned in the first paragraph of this section can be overlooked or neglected if phlebothrombosis is to be prevented. It is shortsighted to treat a weakened heart and at the same time allow fluid to accumulate in the pleural or peritoneal cavities, to fail to relieve abdominal distention from other causes, to neglect the value of deep breathing, to allow extremities to become cold, or to fail to see that gravity and muscular exercise are all highly important means of securing and maintaining normal venous flow from the legs. One need not be so concerned about the arms, for unless the patient is extremely weak the upper extremities will be moved to some extent. But, all too often, the legs are forgotten and allowed to remain motionless, or even worse, are propped up on pillows in a position most comfortable to the patient but dangerous to his welfare.

We believe, in common with many others, that the only sensible approach to the problem of pulmonary embolism is that of prevention of phlebothrombosis whenever the patient is seen from the onset of illness or injury, unless there are very definite contraindications. Comparatively few patients must be kept at absolute bed rest.

One of the first hurdles to clear is the old view that only surgical, accident, and obstetrical patients ever have pulmonary embolism. Nothing could be farther from the truth, as others and ourselves have amply proved. The common denominator in phlebothrombosis and pulmonary embolism is *confinement to bed.* The reason for going to bed is unimportant.

Another step that must be taken if progress is to be made is that of education of medical students, interns, physicians in practice, and nurses. Hereafter the teaching must be that all adults confined to bed are potential subjects of phlebothrombosis and pulmonary embolism. Nursing supervisors, out of training long enough not to have been taught the newer facts, must be so informed. These women stand in a crucial position, for upon their wholehearted cooperation largely depends the success or failure of any regime of treatment. Periodically in every hospital someone should give lectures and demonstrations both to the nurses and to the interns so that with changes in personnel the matter is not forgotten or allowed to lapse.

A simple means of making the hospital "embolism conscious" and of serving as a constant reminder that something is being done to prevent embolism is to hand stamp in large letters on the order sheet of

every chart the words *leg exercises: yes____* or *no____*. Both the stamping and the check mark at the proper point are quickly done and save time. Printed letters are also much easier to read than longhand.

We do not know just how many times each day a bed patient should flex and extend the feet, knees, and thighs, but one thing is certain, namely, that some of the periods of exercise should be made in the presence of the nurse or physician. A convenient time for both is when the temperature is being taken, or at mealtimes. In this way the nurse can observe whether the patient is putting any effort into the exercise or merely playing at moving. Likewise, the intern and the resident should ask the patient to demonstrate his ability to exercise every time rounds are made.

If the cooperation of the patient is to be had, bed exercises must be made comfortable to him. One cannot expect a person to flex vigorously and extend the legs while tightly covered by bed clothing. Many people object to the scratchy sensation of their toenails against the bed sheet and will not move freely under such circumstances. Turning on one side easily obviates the difficulty.

Pillows under the knees for more than a very few minutes at a time should be an absolutely forbidden practice in all hospitals. At best the popliteal space is an anatomic bottleneck and to increase it by flexion and elevation of the knee is wholly unjustifiable.

The modern practice of early rising after operation and the shortening of confinement to bed of medical patients brought about by chemotherapy are undoubtedly doing something to prevent phlebothrombosis, but we must never forget that the process can begin within a very few days so that early rising alone will not insure against thrombosis.

In a recent thought-provoking symposium, Doek and his associates[14] have emphasized not only the frequency of pulmonary embolism originating from leg and pelvic veins of bedridden persons, but other serious effects of confinement as well. His indictment of the abuse of bed rest is a scathing one.

Strange as it may seem, elevation of the head of the bed will effectually cause most patients to exercise their legs. All but the most debilitated have an innate dislike for slipping downward in bed and in bringing themselves back to the head of the bed are forced to put real effort into their legs. When nurses are insufficient, or where patients must be alone, this method has much to commend it.

While it has been shown that thyroid extract will increase metabolism and the circulation time, we have always felt it better to rely on purely physiologic means and not to risk upsetting the balance of the thyroid gland by giving the extract.

SUMMARY

1. A comparative study of the incidence of venous thrombosis of the legs in 400 unselected autopsies on adults, performed in the same hospital, before and after instituting preventive measures is presented.

2. In the last 200 cases dissection of the femoral and adductor veins was carried out. Like others who have examined the femoral vein, we find that phlebothrombosis of the lower extremities begins in the deep vessels of the calf and tends to propagate toward the heart, and that thrombosis of the femoral veins alone is an uncommon occurrence. Both sets of veins are the most frequent, and for this reason the most important, of all the possible sources of both fatal and nonfatal pulmonary emboli.

3. There were no important differences between the two series concerning age, sex, or location of the thrombosed calf veins. The last-mentioned feature has been considered in some detail in a previous publication.[9]

4. Thrombosis of the deep veins of the leg is a frequent event in all classes of middle-aged and older patients who for any reason whatsoever must go to bed for longer than a very few days. The onset is insidious and without prominent symptoms. Phlebitis, as a cause or as a complication of deep extremity vein thrombosis, is very uncommon and for this reason is unimportant.

5. The logical approach to the problem of phlebothrombosis and pulmonary embolism is prophylactic. Hitherto, in our opinion, there has been far too much emphasis upon diagnosis and treatment and too little on prevention.

6. Prophylaxis is best based on simple and readily carried out physiologic principles.

7. Re-education of physicians and nurses with respect to the seats and causes of thrombosis of the legs is urgently needed.

8. The incidence of phlebothrombosis in a small series of medical patients proved to be significantly less than it was in the first 200 cases. It seems probable that the institution of active exercises for this group is responsible for the decrease.

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POSTOPERATIVE PULMONARY EMBOLISM

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PULMONARY embolism commonly is considered an unexpected catastrophy occurring suddenly after some operative procedure, and usually without warning, in a person who had convalesced nicely and was about to be discharged. Often the embolism takes place when the patient is just beginning to resume normal activities, for example, walking or at stool. This conception is only partially true, because embolism is perhaps even more frequent in persons who have been confined to bed for other reasons than an operation, as after delivery, a fracture, particularly of a lower extremity, and in many diseases, especially those associated with an impaired circulation. It may also, on rare occasions, occur in an individual who has not been confined to bed. In many instances there have been warnings as to what might happen—symptoms which, properly considered, might have led one to suspect that a small nonfatal embolism had taken place; for example, such symptoms as a sudden pleuritic pain with or without bloody sputum. Belt[3] and Breslich[4] have shown that pulmonary embolism is even more common in persons dying of medical diseases than in those dying after some operation and is present in some 10 to 12 per cent of routine post-mortem examinations on adults.

In 1846, Virchow[19] published the first correctly interpreted examples of clot embolism of the lungs. Others, previously, had given clear descriptions of it, but did not correctly interpret or understand what had happened. Virchow's idea, that the clot, found obstructing the pulmonary artery, had come from the veins of the pelvis or lower extremities, was bitterly disputed for a long time. He[19a] put his theory to the experimental test and proved that solid masses could be carried by the blood through the veins to the lungs. His cases of embolism occurred, as might be expected, not after operations, but following childbirth, trauma, and disease. When Virchow first wrote on this subject there were none of the present-day surgical procedures except amputations, hence it was not until some decades later that pulmonary embolism began to be considered a postoperative complication or accident. Then its occurrence in nonoperative patients was forgotten to a degree and the broader aspects of the whole problem did not receive deserved attention; in discussion, embolism was, to a great extent, regarded as a surgical calamity. In the century since Virchow gave his clear description, even though papers without number have been written on the subject, much is still to be learned about the underlying causes of thrombosis and embolism and their prevention.

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Pulmonary embolism is always a complication of some pre-existing disease, which has almost always confined the person to bed. When the embolism takes place the symptoms usually come on suddenly. Depending largely upon the size of the embolus or emboli, death occurs quickly, after some minutes, hours, or days. Probably not infrequently the patient recovers completely. The symptoms, in brief, are dyspnea, substernal pain or discomfort, cyanosis, and anxiety. There may be a pleuritic type of pain, vomiting or cerebral symptoms, sometimes with convulsions, or signs of shock and circulatory collapse. If the embolus is massive, occluding the trunk of the pulmonary artery, it may kill in a few seconds. If small, one or more lung infarcts may develop, with or without pleural pain, effusion, or bloody sputum. Infarction often precedes a final fatal embolism. A shower of small emboli may have the same effect as a single large one, interfering either with the free access of blood to the lung, resulting in damage to the lung, or by stasis to the brain. When there is a shower of small emboli, all of them probably do not reach the lung at the same time, but the end result may be the same, although the time from onset to death will probably be much greater. If there is a series of small embolisms, some of the earlier ones to arrive in the lungs may cause infarctions or propagate proximally and bring about the same result as a single large embolus. With an embolism, which is not immediately fatal, pneumonia or coronary disease is often suspected. When either pneumonia or a coronary attack is diagnosed in a convalescent, one should remember that a nonfatal embolism may be the correct diagnosis. Such symptoms may constitute a warning of a fatal embolism to come. McGinn and White[14] and others have shown that by the use of electrocardiography a differentiation may be made between coronary disease and acute cor pulmonale.

Before pulmonary embolism can take place there must be thrombosis of a vein in some part of the body. The common primary sites of thrombosis are the veins of the lower extremities and pelvis, and rarely elsewhere. Small nonfatal emboli not infrequently come from the right side of the heart, usually from the atrium. Embolism usually occurs in individuals who have shown none of the ordinary signs of thrombophlebitis. An unexplained fever or leucocytosis may be the only indication that something is wrong. When an embolus is found at post-mortem examination, one is immediately curious as to its origin. As necropsies are ordinarily done, the site of primary thrombosis is found in only about two-thirds of examinations, although a complete dissection may fail to reveal the source. Perhaps in such instances the entire thrombus had torn loose and a small roughened area on the intima of a vein might be overlooked easily. Massive emboli usually come from the iliac or femoral veins, although the very beginning of the thrombus may have been far down the leg. Hunter and his coworkers[11] have shown at post-mortem examination that in bed patients

in the latter half of life, thromboses are present in the deep veins of the leg in 52.7 per cent of cases. Rössle[17] has found such thrombosed veins in approximately 25 per cent of adults at necropsy. It is often alleged that the primary site of thrombosis is more frequently in the left than the right lower extremity, but there is reason to doubt the truth of this statement. It rarely happens that an embolus has its origin in a vein in the field of operation. When pulmonary embolism occurs after trauma the primary thrombosis may have been in a traumatized vein, but not necessarily so, as it may have arisen in the opposite extremity. In embolism following delivery, the embolus may have come from a vein near the uterus, but again not necessarily so.

The process of thrombosis is closely related to the normal process of coagulation of blood, but normally there is no intravascular clotting during life. If blood did not normally clot after a blood vessel was opened, there could be no successful surgery, because hemorrhage could not be completely stopped, and people would die after trivial cuts. In patients who develop thrombosis, with or without embolism, clotting of the blood goes far beyond the normal limits, and clots form where there has been no obvious injury to a vessel. Why this abnormal clotting takes place is not entirely clear. Many factors apparently operate to cause thrombosis. Usually these factors are divided into three groups: (1) slowing of the blood stream, (2) injury of the endothelium, and (3) changes in the composition of the blood. Which of these is most important we do not know; probably in a given instance one is more important than the others. Slowing of the blood stream, particularly with eddy formation, has long been considered as of prime importance. In my material, venous thrombosis was found five to six times as commonly where chronic passive congestion, as indicated by the liver, was present, as when there was no passive congestion. It is well known that when endothelium is damaged thrombosis may occur. Group 3, changes in the composition of the blood, includes many items, for example, changes in the prothrombin time, clotting time, calcium time, sedimentation rate, platelet count, infection. There are other factors of importance which cannot be placed in any of these groups. These are age, sex, site of operation or injury, disease, obesity, and weather. Advancing age with its gradual loss of muscular tone and relative inactivity may well cause some slowing of the blood stream, even though there is no apparent organic cardiovascular disease. Obesity, likewise, may decrease the rate of flow of the blood stream for the same reasons as advancing age. Enforced bed rest from any cause may slow the blood stream, especially in certain parts of the body. Disease through inactivity or changes in the composition of the blood might promote stasis and thrombosis. An old person with impaired muscular tone and cardiovascular system should be a much more likely candidate for thrombosis and embolism than a young person with good muscular tone and a sound cardiovascular system, if

each was subjected to the same operation or trauma. If advanced age, obesity, impaired cardiovascular system, disease, and operation occur in the same person the likelihood of thrombosis may be still greater. It would appear that thrombosis and embolism may be due to a number of variables, operating in different combinations in different persons.

Aschoff's[1] theory of thrombosis is the one most generally accepted, although in recent years some opposition to it has arisen. According to Aschoff, fatal emboli come from thromboses of the iliac or femoral veins. The thrombus usually begins near a vein valve as a platelet or agglutination thrombus and this forms the head or *Kopfteil*. When this platelet thrombus has become large enough to occlude the vein, then a coagulation thrombus made up of fibrin, red blood cells, and leucocytes forms in the obstructed vein where the blood is at a standstill. In recent years, due to the studies of Olow,[16] Denecke,[6] Rössle,[17] Neumann,[15] Frykholm,[9] and others, evidence has accumulated indicating that the thrombosis, with or without embolism, actually may have started in the deep veins of the calf of the leg or foot. Then by propagation and accretion the thrombus may have extended up the veins of the lower extremity, not occluding the lumens, but waving freely in the passing blood. It has been suggested that compression of the veins during rest in bed may have caused empty veins to be flattened and the so-apposed endothlial linings to be damaged. Such a focus of endothelial injury might be the site for the initiation of a thrombus.

It is very difficult to work out the real incidence of thrombosis and embolism for many reasons. Autopsy material should give accurate information on this subject, if complete post-mortem examinations were done routinely. Unfortunately, necropsies are done on only a fraction of those who die in any community or hospital, and at best give information only on those examined. Hospital populations vary from hospital to hospital in age, sex, type of disease, economic status, etc.

Reports from various sources show an incidence of from less than 1 to almost 12 per cent in routine autopsies. Domrich[8] in 26,439 necropsies found pulmonary embolism in one-half of 1 per cent and in another series of 2,500 examinations an incidence of 2.4 per cent. Belt[3] in 567 examinations found emboli in 9.8 per cent of persons and Breslich[4] in 457 necropsies found embolism in 11.8 per cent. A serious difficulty encountered in trying to compare the data of different authors is that often the age distribution of all the patients on whom post-mortem examinations were made is not given. A series derived from nonsurgical deaths cannot be compared with a series from a surgical service. Another difficulty found in trying to make comparisons is that many authors have drawn no distinction between fatal and nonfatal embolisms. The incidence of thrombosis and embolism based entirely on clinical data is open to obvious objections.

Similarly in reports on the incidence of thrombosis and embolism following surgical procedures, there is great variation ranging from 0.02 to almost 1 per cent. In 1912, Wilson[20] reported on 63,753 operations done at the Mayo Clinic and found an incidence of embolism of 0.07 per cent. Heard,[10] in 1923, at the Mayo Clinic found an incidence of embolism of 0.12 per cent in 60,757 operations on men and of 0.07 per cent in 43,605 operations on women. In 1940, Barker and his collaborators,[2] also reporting from the Mayo Clinic, showed an incidence of thrombosis and embolism of 0.96 per cent in 172,888 operations, of pulmonary embolism of 0.52 per cent, and of fatal embolism of 0.20 per cent. They have analyzed their material according to site of operation and magnitude. They found that the incidence of fatal pulmonary embolism varied from 0 to 0.77 per cent. All of these series have come from the same clinic and yet there is a difference in incidence. It might appear that these series are really comparable, but yet they may not be at all similar. It might appear that embolism had increased in frequency at the Mayo Clinic, but it is doubtful whether such a conclusion is really justified.

Numerous articles have been written to show that thrombosis and embolism have increased since World War I. Part of this apparent increase can probably be referred to comparisons of dissimilar data. From perusal of articles written since Virchow's description it would appear that the incidence of embolism has followed a wavelike course. Virchow reported one of the highest incidences of embolism, having found pulmonary embolism eleven times in seventy-six post-mortem examinations.

My data are based on 25,771 necropsies done by the department of pathology of the University of Minnesota during the twenty years from Jan. 1, 1919, to Dec. 31, 1938. From the autopsy records I determined that in 689 instances, or 2.67 per cent, death was to be attributed to pulmonary embolism. This appears to be but one-fourth the incidence as determined by Belt and Breslich. However, in my opinion this difference in incidence is to be explained by the fact that they were considering all pulmonary embolisms, fatal and nonfatal. Their conception, while broader than mine, is still not broad enough. To get a full view of the problem we must broaden the base to include not only the cases where pulmonary embolism actually occurred, but also those instances where it might have taken place, because venous thrombosis was present. The embolism was merely a fortuitous event. When a thrombus forms in a vein, the bearer of that vein is in line to be a victim of pulmonary embolism. From this point of view there was, in my material, embolism or the possibility of embolism in 10 per cent of the autopsies. If the cases of venous thrombosis without embolism be deducted, then pulmonary artery thrombosis or embolism occurred in 7.2 per cent, a figure not too far from those of Belt and Breslich. The difference may be due to differences in the sources from

which the material was obtained. My material came from private and charity hospitals, the coroner's service, and the private practices of physicians. It represents about 16 per cent of the deaths in Minneapolis, but included are necropsies done on persons who had died elsewhere. The age distribution in these examinations closely follows the curve of vital statistics as to decade distribution of deaths.

Much has been written to show that pulmonary embolism has a seasonal incidence. De Takats and his co-workers[7] studied 100 cases of pulmonary embolism and found the greatest incidence during the spring and fall, the times of the year with the greatest fluctuations in barometric pressure and temperature. Martland[12] found that in 86 massive embolisms in 10,797 necropsies from his medical examiner's service, March, April, September, and December were the months with the greatest incidence of pulmonary embolism. My material covering a twenty-year period shows that month by month and year by year the number of examinations runs at a fairly uniform level, although the number of examinations has gradually increased. The incidence of thrombo-embolism has also followed a uniform course and there are no indications of a seasonal influence.

Consideration of the decade distribution of the present series of post-mortem examinations and the occurrence of thrombo-embolism in the various decades showed that thrombosis and embolism occurred at all ages with a tendency to a greater incidence as age advanced. This was true whether fatal embolism or venous thrombosis with or without embolism was considered. This effect of age is shown in Table I and particularly with fatal embolism there is a steady rise from the first to the ninth decades. Perhaps the frequency of thrombosis in the first decade may be referred to infections, such as those of the middle ear. Puerperal infection doubtless increases the incidence of thrombo-embolism during the childbearing period, although fatal embolism after delivery is infrequent. Nevertheless, fatal pulmonary

TABLE I

AGE DISTRIBUTION OF 25,771 NECROPSIES AND INCIDENCE OF THROMBO-EMBOLISM AND FATAL EMBOLISM IN EACH DECADE

DECADE	NUMBER	THROMBO-EMBOLISM (PER CENT)	FATAL EMBOLISM (PER CENT)
1	3,277	3.1	0.18
2	1,050	9.7	0.57
3	1,945	9.4	1.49
4	2,676	9.0	2.09
5	3,818	10.6	2.46
6	4,157	12.2	3.31
7	4,196	12.4	3.95
8	2,908	14.1	4.74
9	816	13.6	5.39
10	54	12.9	1.84
Adults	874		
Total	25,771	10.1	2.67

embolism is notably higher in women after delivery than in those dying during the childbearing period.

From earlier studies[13] it appeared that fatal embolism was more common in men, but after fatal trauma more common in women. Barker and co-workers found thrombosis and embolism to be relatively more common in women than in men, but fatal embolism more frequent in men. The present study indicates that thrombo-embolism and fatal embolism are more common in women, thrombo-embolism occurring in 9.1 per cent of men and in 11.2 per cent of women, and fatal embolism in 2.2 per cent of men and 3.3 per cent of women. (In this calculation post-partum cases were excluded, because of this special condition.)

In order to study another factor which might play a part in thrombo-embolism, this material was divided according to anatomically normal and abnormal hearts. This analysis showed that in persons with heart disease, thrombosis and embolism occurred approximately three times as often as it did in persons with normal hearts. Further subdivision of these two groups by age revealed that in persons with anatomically normal hearts there was a slight but gradual increase of thrombosis and embolism as age advanced, whereas in persons with diseased hearts thrombo-embolism occurred fairly uniformly in all decades of life, except the first. As just indicated, when the liver showed chronic passive congestion, venous thrombosis was five to six times as common as it was when the liver appeared normal.

Thrombo-embolism may be divided readily into postoperative, post-traumatic, post-partum, and medical groups. When thus divided I found, for these groups, incidences of 5.4, 3.5, 4.7, and 1.2 per cent respectively. A statistical determination of the significance of these differences in percentage has not been made. In all of these four groups, when divided according to age, there appeared to be a definite age effect, with an increasing occurrence of thrombo-embolism with advancing age.

A discussion of postoperative thrombosis and embolism, to which objections cannot be raised, requires much more data than are usually given. It is necessary to know not only the number of operations according to sites, but also the sex, the ages at which the various operations have been done, the postoperative mortalities by decades, and, if post-mortem examinations were not made, then the clinical causes of death should be included. Such information I have not as yet been able to find. This information is needed before there is justification for claiming that certain operations are more likely than others to be followed by thrombo-embolism. It may be true, but the reasons and the foundations for the statements do not appear. To state that pulmonary embolism occurs more commonly after certain operations and in the latter half of life is a commonplace, but this truism is usually not investigated further and the reasons and causes

for any such greater occurrence have not been found. Among the contributors to the higher incidences of pulmonary embolism are mentioned operations on the bladder and prostate. A moment's reflection suggests that the reason for this may be that such operations are done only rarely in the early decades of life. It is often said that appendectomy is a large contributor to embolism in early life. The obvious reason for this is that most of the primary appendectomies are done during the first three decades of life and with the large numbers of appendectomies done, the chances for embolism to occur are increased, even though the actual incidence may be very low. Why herniorrhaphy should so often, as is alleged, be followed by thrombosis or embolism is not clear, but, as in the case of the appendix, it may be related to the time of life when most hernioplasties are done.

Barker and his collaborators, in their study of 172,888 operations, divided them according to site and magnitude of operation. They found "venous thrombosis and pulmonary embolism are relatively twice as common following laparotomy as they are following all operations and they are three times as common following laparotomy in which operations on the female pelvic organs were done as they are following all operations. The highest incidence of venous thrombosis and pulmonary embolism occurs in operations where there is laparotomy and extensive resection of tissue. These are operations which can be considered to be of relatively long duration and of relatively great magnitude. The incidence of venous thrombosis and pulmonary embolism is approximately twice as great in cases of repair of bilateral femoral or inguinal hernia as in cases of unilateral femoral or inguinal hernia. Here the difference is only that of magnitude and duration of operation." They call attention to the high incidence after splenectomy, and believe it is in some way related to the blood changes associated with the reasons for splenectomy. Their data are tabulated under four heads, namely, all thrombosis and embolism, pulmonary embolism, fatal pulmonary embolism, and clinical diagnosis of thrombophlebitis. Rearrangement of these data gives some interesting results. Splenectomy takes first place three times in these four items and second place once. Abdominal hysterectomy takes first place, once; second place, twice; and sixth place, once. Third place is taken twice by cesarean section and once each by resection of the intestine and other intestinal operations. Fourth place is taken once by other intestinal operations, once by bladder and prostate operations, once by exploratory laparotomy for inoperable malignant lesion, and once by bilateral femoral or inguinal hernia operations. Twice colostomy and/or enterostomy assumes fifth place, and once each this place is taken by bilateral femoral or inguinal hernia and vaginal hysterectomy. Sixth place falls twice in the column of resection of the stomach and once each in abdominal hysterectomy and other intestinal operations. Seventh place is taken once each by cesarean section, bilateral femoral or inguinal hernia operation, intestinal resection, and other gynecologic operations.

Eighth place falls once in the column of vaginal hysterectomy, once in appendectomy for ruptured appendix, once in bilateral femoral or inguinal hernia, and once in other hernia except diaphragmatic. Ninth place is twice in the column for resection of the stomach, once in prostate and bladder, and once in colostomy or enterostomy. In tenth place are colostomy or enterostomy, exploratory laparotomy for inoperable malignant lesion, other lower abdominal operations, gall bladder and duct, and other stomach operations. This survey might be continued through all the thirty-six types or locations of operations tabulated by the authors. This much reveals that thrombo-embolic disease tends to occur particularly after operations on special sites, without any apparent explanation, save that, with the exception of vaginal hysterectomy, the chief contributors involved incision into or through the anterior abdominal wall. Their table also shows that no part of the body was free of its complement of postoperative thrombo-embolism. Culp,[5] in a survey of 8,163 urologic operations, found 88 pulmonary embolisms of which 32 were fatal and so proved at necropsy. There were 11 presumptive embolisms, 21 infarcts with recovery, and 4 infected infarcts. He states that embolism was responsible for 6.62 per cent of all postoperative deaths. He also noted that 81.2 per cent of the embolisms were in private patients, and the only difference between private and ward patients that he could find was that the former tended to be overweight and the latter underweight. Of the embolisms, 62.5 per cent were in persons over 60 years of age, whereas only 41.2 per cent of all patients were over 60 years of age. Further, while 25 per cent of fatal embolisms were in persons from 71 to 80 years of age, only 12.5 per cent of all patients were of this age. Of the patients with embolism, 31 per cent were of normal height, 43.7 per cent underweight, and 25 per cent overweight. The incidence of fatal embolism after suprapubic operations was 0.67 per cent, after perineal 0.57 per cent, and after transurethral 0.25 per cent. There was marked abdominal distention in 43.8 per cent, which might have increased stasis of blood in the pelvis or lower extremities. There was clinical evidence of cardiac decompensation preoperatively in 20 per cent, another 10 per cent had high diastolic pressures, and another 40 per cent had myocardial scarring at post-mortem examination. Clinical thrombosis was present in 18.8 per cent. Veal,[18] in a study on femoral vein ligations to prevent pulmonary complications after thigh amputations, concludes that "pulmonary complications are more frequent following thigh amputations than in any other field of surgery. Many of the pulmonary lesions are embolic in origin." All of these indicate that it is necessary to know more about the operative procedures than their site and magnitude. Knowledge as to age at which operations are done as well as mortality by decades might furnish useful information in an attempt to learn the factors which underlie thrombo-embolism.

To get some information on the question of when various operations are done, I have gathered from the literature data bearing on this point. These data show that for the appendix about three-fourths of the primary appendectomies are done before the age of thirty years; about one-half of the herniorrhaphies are done during the first three decades; about 85 per cent of gall bladder operations are done after the age of 30 years, more than one-half between the ages of 30 and 49 years, and less than one-third after the age of 50 years. Apparently about one-half of the abdominal gynecologic operations are done during the fourth and fifth decades, and only about 20 per cent after the age of 50 years; until the fifth decade there are almost no suprapubic operations on the bladder and prostate; about 75 per cent of operations on the head and neck are done during the first three decades of life. This by no means covers all the operative fields, but is a clear indication that age must be given full consideration before a true comparison can be made as to the relative incidence of thrombo-embolism as a complication following operations on particular sites.

Of the 25,771 autopsy records studied, I decided that 4,070 were to be classified as postoperative deaths. In this group venous thrombosis or pulmonary embolism was found in 471 instances or in 11.5 per cent. I considered that in 216 instances the pulmonary embolism could be called fatal, that is, in 5.3 per cent of cases. There were 1,506 women with 182 thromboses and embolisms, or 12.0 per cent, and 2,564 men with 281 instances of thrombo-embolism, or 10.9 per cent. In the 1,506 women there were 90 fatal embolisms, or 5.9 per cent, and in the 2,564 men 126 fatal embolisms, or 4.9 per cent.

Table II indicates that the ages in the routine autopsies and in those done after postoperative deaths are approximately the same. The actual number of autopsies in each decade done on persons dying after operation is given at the end of Table III. In the same place are given the incidences of thrombo-embolism and fatal embolisms. If it may be assumed that such distribution of postoperative deaths is true, then it is clear that while thrombosis and embolism occur in all decades there is a tendency for them to increase in frequency with age. This is even truer of fatal embolism. It is worthy of note that only 11, or

TABLE II

AGE DISTRIBUTION OF AUTOPSIES (24,927 ROUTINE AND 4,040 POSTOPERATIVE)

DECADE	ROUTINE	POSTOPERATIVE
1	13.1	10.2
2	4.2	5.5
3	7.8	7.4
4	10.7	10.0
5	15.3	12.4
6	16.6	18.6
7	16.8	18.5
8	11.6	11.6
9	3.2	2.4

5 per cent, of the 214 fatal embolisms considered as fatal occurred in patients before the age of 30 years, and that only 31, or 14.4 per cent, were in persons under 40 years of age, whereas 23.2 per cent of all postoperative thromboses and embolisms were in persons under 40 years of age.

Table III shows the age, site of operation, and incidence of thrombo-embolism and fatal embolism, in the 4,070 necropsies in persons dead after operation. The operative sites were associated with thrombo-embolism and fatal embolism in the actual numbers as shown in Table IV, and the incidence of thrombo-embolism and fatal embolism as complications of these various sites is shown in Table V. (In these tables suprapubic operations on the bladder and/or prostate are all included under bladder, and the transurethral prostatectomies under perineum.)

The relatively high incidence of thrombosis, with or without embolism, after operations on the head is doubtless related to infection, for example, otitis media and mastoiditis. It may be noted in Table III that of the 391 operations on the head, 165 were done in patients under the age of 20 years and 207 in those under the age of 30. Of the fifty-eight instances of thrombo-embolism after head operations thirty-three were in persons under 30 years of age. All of these thirty-three were associated with infection. There were five fatal embolisms after head operations and all were in persons over 50 years of age. These five embolisms give an incidence of 1.2 per cent for persons dying after head operations. Operations on the extremities were the second largest contributor to the actual number of instances of thrombo-embolism, but ranked in eighth place in the number of fatal embolisms. Fatal embolism occurred in only 5.5 per cent of persons, but the possibility of embolism was present in 20 per cent. It is to be noted in Table III that thrombo-embolism and fatal embolism occurred in all but two of the decades (third and fifth), and that here there is no evidence of an increased incidence with age.

Suprapubic operation on the bladder and/or prostate was in third place in the actual number of thrombo-embolisms and in second place in the number of fatal embolisms. Thrombo-embolism occurred with the possibility of fatal embolism in 15.5 per cent of persons and such fatal embolism took place in 10.3 per cent of individuals. In Table III it will be noted that no thrombosis or embolism was found before the fifth decade in any person who had undergone an operation on these organs, further that all the fatal embolisms occurred after the fifth decade of life. Of the 270 operations in this category, 9 were in women with neither thrombosis nor embolism. Of the twenty-eight fatal embolisms in men, all but one occurred after the sixth decade. Sixteen of these followed prostatectomy and twelve followed various operations on the bladder. Fifteen showed normal hearts and thirteen some evidence of organic heart disease. It may be mentioned here that in forty-one deaths following transurethral resection of the prostate there

TABLE III

AGE, SITE OF OPERATION, AND INCIDENCE OF THROMBO-EMBOLISM AND FATAL EMBOLISM IN 4,070 POSTOPERATIVE NECROPSIES

DECADE	1	2	3	4	5	6	7	8	9	10	UNKNOWN	TOTAL
Site												
Head	110	55	42	38	42	39	32	19	5			391
T.E. %	10.0	21.8	23.8	13.1	14.2	15.4	9.3	22.2	20.0			14.8
Emb. %						2.5	6.2	5.2	20.0			1.2
Neck	53	12	11	27	32	46	51	21	3		2	258
T.E. %		25.0			15.5	15.2	3.9	9.5				7.3
Emb. %					3.1		1.9	4.7				1.1
Thorax	26	15	36	38	49	34	13	3	1			215
T.E. %		20.0	11.1	18.4	1.0	5.8	15.3					10.2
Emb. %			2.7	7.9		5.8						2.7
Spine	13	10	3	8	3	9	2	2	1			54
T.E. %					33.3							1.8
Emb. %												0
Expl. lap.	52	17	34	53	75	87	81	41	3		6	450
T.E. %	3.8	11.7	5.8	3.7	4.0	6.8	8.6	2.4	33.3			5.7
Emb. %			2.9	1.8	1.3	3.4	3.7					2.0
Stomach	34		9	18	55	93	82	51	6		4	352
T.E. %				5.5	3.6	4.3	8.5	9.8	16.6			5.6
Emb. %						2.1	2.4	3.9	16.6			1.9
Small int.	8	9	13	38	48	40	44	20		1	2	223
T.E. %			7.6	7.8	10.4	10.0	4.5	10.0				7.6
Emb. %			7.6	7.8	4.1	2.5	2.2	5.0				4.0
Large int.	8	5	8	13	40	78	94	39	10			295
T.E. %			12.5	7.6	15.0	14.1	13.9	5.1				11.5
Emb. %					5.0	5.1	9.5	2.5				5.4
Gall bladder			13	27	56	74	77	30	1		2	280
T.E. %				7.4	14.2	8.1	11.6	10.0				10.0
Emb. %				3.7	10.7	6.7	10.3	6.6				7.8

Appendix	29	57	56	41	43	44	23	14			2	309
T.E. %	3.4	3.5	7.1	17.0	13.9	13.5	21.2	14.2				10.6
Emb. %		1.7	7.1	7.3	4.6	9.0	17.2	7.1				6.1
Spleen	3	4	1	4	3	5		1				21
T.E. %												0
Emb. %												0
Hernia	7		3	7	17	33	33	16	8		4	128
T.E. %				14.2	29.4	24.2	42.1	12.5	37.5		50.0	24.2
Emb. %				14.2	23.5	21.2	33.3	12.5	25.0		50.0	22.6
Adnexa		6	23	18	19	8	5	3	1		1	84
T.E. %			8.6	11.1	10.5	12.5	20.0					9.5
Emb. %			4.3	11.1	5.2	12.5	20.0					7.1
Uterus		2	14	28	36	16	7	2			1	106
T.E. %			14.2	10.7	36.1	31.2	42.8	50.0				25.4
Emb. %				10.7	25.0	25.0	28.5	50.0				17.9
Bladder and prostate	4	1	1	2	12	35	80	96	36		1	270
T.E. %					8.3	8.5	18.7	14.5	25.0			15.5
Emb. %						2.8	13.7	9.3	19.4			10.3
Perineal	9	4	11	11	21	36	46	64	17			222
T.E. %			9.0		9.5	16.6	23.9	17.1	11.7			14.8
Emb. %					4.7	8.3	13.0	7.8	11.7			7.6
Kidney	5	1	8	14	21	25	24	10			1	109
T.E.%			25.0	7.1	4.7	20.0	16.6	10.0				12.8
Emb. %				7.1	4.7	8.0	12.5					6.4
Extremity	30	22	10	12	26	41	50	33	7		4	235
T.E. %	16.6	31.8	10.0	25.0	19.2	17.0	20.0	21.2	14.2			20.0
Emb. %	3.3	4.5		8.3		12.1	6.0	6.1				5.5
Misc.	14	5	3	10	5	10	5	4	1			68
T.E. %		20.0	66.6	20.0		10.0	20.0					10.2
Emb. %				10.0								1.4
Total	405	225	299	407	503	753	749	469	100	1	30	4070
T.E. %	4.6	13.3	10.3	10.0	14.9	11.6	14.6	11.9	16.0		6.6	11.5
Emb. %	0.24	0.88	2.67	4.91	5.96	5.71	9.21	5.97	13.0			5.30

TABLE IV

ACTUAL NUMBERS OF THROMBO-EMBOLISMS AND FATAL EMBOLISMS ACCORDING TO OPERATIVE SITES

THROMBOSIS AND EMBOLISM	NUMBER	FATAL EMBOLISM	NUMBER
Head	58	Hernia	29
Extremity	47	Bladder	28
Bladder	42	Gall bladder	22
Hernia	35	Appendix	19
Large intestine	34	Uterus	19
Appendix	33	Perineum	17
Perineum	33	Large intestine	16
Gall bladder	28	Extremity	13
Uterus	27	Small intestine	9
Exploratory laparotomy	26	Exploratory laparotomy	9
Thorax	22	Stomach	7
Stomach	20	Kidney	7
Neck	19	Thorax	6
Small intestine	17	Adnexa	6
Kidney	14	Head	5
Adnexa	8	Neck	3
Miscellaneous	7	Miscellaneous	1
Spine	1	Spine	0
Spleen	0	Spleen	0

were seven instances of fatal pulmonary embolism, all in individuals with heart disease. This is an incidence of 17 per cent, which is more than twice the incidence for the whole perineal group.

The 128 operations for hernia yielded the greatest number of fatal embolisms, and herniorrhaphies ranked first among the operative sites having this complication and cause of death. As will be seen in Table III, no thromboses or fatal embolisms occurred in patients under the age of 30 years and the highest incidences of thrombo-embolism and fatal embolism were found in the seventh decade of life.

TABLE V

INCIDENCE OF THROMBO-EMBOLISM AND FATAL EMBOLISM ACCORDING TO OPERATIVE SITES

THROMBO-EMBOLISM	PER CENT	FATAL EMBOLISM	PER CENT
Uterus	25.4	Hernia	22.6
Hernia	24.2	Uterus	17.9
Extremity	20.0	Bladder	10.3
Bladder	15.5	Gall bladder	7.8
Perineum	14.8	Perineum	7.6
Head	14.8	Adnexa	7.1
Kidney	12.8	Kidney	6.4
Large intestine	11.5	Appendix	6.1
Appendix	10.6	Extremity	5.5
Miscellaneous	10.2	Large intestine	5.4
Thorax	10.2	Small intestine	4.0
Gall bladder	10.0	Thorax	2.7
Adnexa	9.5	Exploratory laparotomy	2.0
Small intestine	7.6	Stomach	1.9
Neck	7.3	Miscellaneous	1.4
Exploratory laparotomy	5.7	Head	1.2
Stomach	5.6	Neck	1.1
Spine	1.8	Spine	0
Spleen	0	Spleen	0

Operations on the large intestine took fifth place in the list of possibilities for fatal embolism and seventh place in the number of fatal embolisms actually produced. Thus, large intestinal operations had fatal embolism in 5.4 per cent of cases. In Table III it may be seen that there was no instance of fatal embolism, after operation on the large intestine before the fifth decade of life. The peak of incidence for thrombo-embolism was in the fifth decade and the peak for fatal embolism in the seventh decade.

Biliary tract operations produced the third greatest number of fatal embolisms and this was the cause of death in 7.8 per cent of persons after such operations. Thrombo-embolism and fatal embolism first appear in the fourth decade. The decades where these are found show no definite peak in any decade.

Uterine and appendical operations tie for fourth place in the number of fatal embolisms found, although the possibilities for fatal embolism might seem to have been greater for the latter than the former. This does not appear to be true, as is shown in Table V, where thrombo-embolism was present in 25.4 per cent of uterine operations and in but 10.6 per cent of appendical operations. Likewise embolism was fatal in 17.9 per cent of the deaths following uterine operations and caused death in but 6.1 per cent after operations on the appendix. It is to be noted in Table III, regarding the appendix, that embolism appeared first in the second decade and reached its peak in the seventh decade of life, whereas no fatal embolism after a uterine operation was observed until the fourth decade. In both instances there is evidence of an increased incidence of thrombo-embolism and fatal embolism with advancing age.

As may be seen from Tables III, IV, and V, thrombo-embolism and fatal embolism may follow operations on almost any part of the body, but the occurrence of these complications is less frequent than with those just discussed. Examination of Table III will show that for most parts of the body the incidences of thrombo-embolism and fatal embolism increase with the age of the patient.

While it may be correct to say that certain operations are those most likely to be followed by pulmonary embolism, inspection of Tables III, IV, and V will indicate that before such a statement is made certain information aside from the site of operation must be considered. Two of these other considerations are very definitely age and sex.

SUMMARY

A study of 25,771 autopsy records at the University of Minnesota has revealed that 4,070 of the deaths may be considered as postoperative. Among these, postoperative deaths there were 471 instances, or 11.5 per cent, where thrombo-embolism was present and 216, or 5.3 per cent, where it was believed that pulmonary embolism was to be considered as the cause of death.

Analysis of this material according to sites of operation, age, and sex showed (1) that in most parts of the body the incidence of venous thrombosis, with or without pulmonary embolism, and of fatal pulmonary embolism showed a tendency to increase with age, (2) that while thrombosis or embolism might occur following operation on any part of the body, it appeared to be more frequent after operations on certain parts of the body, (3) that age and sex must be given due consideration before a statement as to frequency of embolism is made, and (4) that perhaps the age of the patient at the time of operation may be of as great importance as the site of operation in determining whether thrombosis and embolism will occur.

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THE USE OF DICUMAROL IN THE PREVENTION OF POSTOPERATIVE THROMBOSIS AND EMBOLISM WITH SPECIAL REFERENCE TO DOSAGE AND SAFE ADMINISTRATION

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SINCE the isolation and synthesis of dicumarol [3,3′-methylene-bis-(4-hydroxycoumarin)] by Link and his associates,[1, 2] the action and clinical effects of this drug on human beings have been reviewed in several reports.[3-5] When dicumarol is administered orally, prothrombin deficiency results. Excessive and prolonged prothrombin deficiency produced by frequent large doses of the drug may, but does not certainly, lead to severe hemorrhage. Moderate prothrombin deficiency produced by dicumarol appears to be effective in the prevention of venous thrombosis and, therefore, embolism among postoperative patients.

This report is based on observations of 1,000 surgical patients who were given dicumarol‖ in their immediate postoperative period for the purpose of preventing venous thrombosis and pulmonary embolism. Of these 1,000 patients, 624 were the subject of a previous report.[6]

In the entire series of 1,000 cases there was only one death from pulmonary embolism and in this case, which was early in the study, the embolism occurred after the prothrombin had returned to normal because the dicumarol had been given for insufficient time. The extremely low incidence of fatal pulmonary embolism in 1,000 postoperative cases would not be remarkable if the cases had been unselected, but most of them had been selected. A thrombotic tendency had already been demonstrated in 379 patients in that they had had thrombosis or embolism, and on 438 abdominal hysterectomy had been performed, an operation in which the statistical risk of thrombosis and embolism is known to be greater than in most operations.

CLINICAL RESULTS OF USE OF DICUMAROL

Nonfatal Pulmonary Embolism and Infarction.—The incidence of subsequent venous thrombosis, subsequent pulmonary embolism and infarction, and subsequent fatal embolism among patients to whom dicumarol was administered as compared with a control series from a

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TABLE I

NONFATAL POSTOPERATIVE PULMONARY EMBOLISM AND INFARCTION

	CONTROL GROUP: ANTICOAGULANTS NOT ADMINISTERED		DICUMAROL ADMINISTERED	
	NUMBER	PER CENT	NUMBER	PER CENT
Total cases	678	100	180	100
Subsequent venous thrombosis, pulmonary embolism, or infarction	297	43.8	2*	1.1
Subsequent fatal pulmonary embolism	124	18.3	1†	0.6

*Both when prothrombin was greater than 30 per cent.
†After prothrombin had returned to normal.

previous study[7] is given in Table I. The difference in incidence is striking and, as indicated, there was no recurrence of thrombosis or embolism when the prothrombin deficiency was adequately maintained.

Thrombophlebitis.—In the group of cases in this study no attempt was made to distinguish between phlebothrombosis and thrombophlebitis, since we feel that although the lesion starts with a thrombus, some degree of phlebitis is also present when the diagnosis is made clinically. Some or possibly all of these cases might be classified as phlebothrombosis by those who attempt to make the distinction. Of the 138 cases of thrombophlebitis in which dicumarol was administered, the lesion was in the iliofemoral vein in 67, the veins of the calf in 49, the lower femoral and popliteal in 10, superficial varices in 8, the long saphenous in 3, and the subclavian in 1. In Table II a comparison of incidence of

TABLE II

POSTOPERATIVE THROMBOPHLEBITIS

	CONTROL GROUP: ANTICOAGULANTS NOT ADMINISTERED		DICUMAROL ADMINISTERED	
	NUMBER	PER CENT	NUMBER	PER CENT
Total cases	897	100	138	100
Subsequent episode of thrombophlebitis	95	10.6	4*	2.9
Subsequent fatal pulmonary embolism	51	5.7	0	0

*In two of these cases prothrombin was greater than 30 per cent when thrombophlebitis developed.

subsequent thrombophlebitis and subsequent fatal embolism is given with a control series, not treated with dicumarol, from a previous study.[7] It is of interest that no instance of pulmonary embolism, fatal or nonfatal, occurred among any of the 138 patients treated with dicumarol. This is evidence that when thrombophlebitis is diagnosed clinically the thrombus which is present will almost certainly not detach and become an embolism. The danger from embolism in these cases occurs if a fresh thrombus suddenly propagates into a more proximal vein or if a fresh thrombus develops in a remote vein. If the development of such fresh thrombi is prevented, embolism can be prevented.

History of Thrombophlebitis or Embolism Previous to Operation.—Sixty-one patients with a history of thrombophlebitis or embolism previous to operation were given dicumarol beginning on the second postoperative day. In no case did embolism, fatal or nonfatal, develop. In two cases minor thrombophlebitis developed in superficial varices, but in both the prothrombin deficiency was inadequate (prothrombin content of plasma greater than 30 per cent of normal). No other instances of thrombosis developed.

Prophylaxis After Abdominal Hysterectomy.—Four hundred thirty-eight patients on whom abdominal hysterectomy had been performed and who had not had thrombophlebitis or embolism were given dicumarol for prophylactic purposes beginning on the second postoperative day. This group was selected because of the relatively high risk, compared with those on whom other operations are performed, of postoperative thrombophlebitis and embolism (4 per cent) and fatal embolism (0.7 per cent), as noted in a previous study.[8] No embolisms developed in the cases in which dicumarol was given. In two cases thrombophlebitis of veins of the calf developed after the patients had left the hospital and after the prothrombin had returned to normal. No other thrombophlebitis developed.

Prophylaxis After Other Operations.—Cases in which prophylaxis was given after other operations comprised the remaining 183 patients. No thrombophlebitis or embolism developed in these cases but the group is too small to permit statistical comparison with similar cases in which treatment was not given.

RISK OF BLEEDING AMONG POSTOPERATIVE PATIENTS AFTER ADMINISTRATION OF DICUMAROL

The only hazard in the administration of dicumarol to postoperative patients is the risk of bleeding and we believe that it has been overemphasized. In Table III the incidence of bleeding in the 1,000 cases

TABLE III

INCIDENCE OF BLEEDING AMONG PATIENTS TREATED POSTOPERATIVELY WITH DICUMAROL

REASONS FOR DICUMAROL THERAPY	TOTAL NUMBER OF PATIENTS TREATED	MINOR BLEEDING		MAJOR BLEEDING	
		NUMBER	PER CENT OF TOTAL	NUMBER	PER CENT OF TOTAL
Postoperative pulmonary embolism	180	5	2.8	2	1.1
Postoperative thrombophlebitis	138	5	3.6	1	0.7
History of thrombosis or embolism at any time prior to immediate operation (prophylaxis)	61	1	1.6	1	1.6
Abdominal hysterectomy (prophylaxis)	438	20	4.6	12	2.7
Other operations (prophylaxis)	183	8	4.4	9	4.9
Total	1,000	39	3.9	25	2.5

is given. It will be noted that the incidence is very small among those patients who have already demonstrated a tendency to thrombosis. The total incidence of bleeding has been definitely smaller during the past two years than it was before since we have become more familiar with dosage and prevention and control of excessive and prolonged prothrombin deficiency. Minor bleeding, as mentioned in Table III, consisted of mild epistaxis, microscopic hematuria, and slight oozing from wounds, which may or may not have been caused by the prothrombin deficiency. Major bleeding, when it occurred, almost always came from surgical wounds, particularly the vaginal wound among patients on whom total abdominal hysterectomy had been performed. It was frequently controlled after one transfusion of blood or by intravenous injection of 64 mg. of menadione bisulfite. In a few cases repeated transfusions were necessary. One patient, who had a carcinoma of the third portion of the duodenum which entailed extensive resection with some trauma of the superior mesenteric vein and who was having continuous gastric drainage, was given dicumarol to prevent mesenteric thrombosis. However, only minimal prothrombin deficiency was produced, probably because of poor absorption of the drug. This patient had a massive, fatal gastrointestinal hemorrhage. It is unlikely that the prothrombin deficiency produced or even aggravated the bleeding in this case. No other cases of fatal bleeding occurred among the 1,000 patients treated. In almost all instances of major bleeding the prothrombin was less than 10 per cent of normal when the bleeding occurred. We feel that, if contraindications to the use of dicumarol are observed and there is careful individualization of dosage so that excessive prothrombin deficiency does not develop or is quickly controlled if it does develop, the danger of bleeding is very small.

CONTRAINDICATIONS

On the basis of our experiences we feel that the following conditions constitute definite contraindications to the use of dicumarol: (1) the presence of definite renal insufficiency; (2) the presence of definite hepatic insufficiency or hepatogenous jaundice, particularly if associated with prothrombin deficiency; (3) subacute bacterial endocarditis; (4) purpura of any type; (5) blood dyscrasia with tendency to bleed, and (6) recent operation on the brain or spinal cord. Dicumarol should be given cautiously to patients who have (1) ulcerative lesions, open wounds, or potentially bleeding surfaces; (2) vomiting due to gastric or intestinal obstruction; (3) continuous or repeated gastric or intestinal drainage, or (4) dietary or nutritional deficiency. If an operation is contemplated, ample time should be available for return of prothrombin to normal if dicumarol is administered before the operation. If emergency operation is necessary on a patient who has prothrombin deficiency owing to dicumarol, large doses of menadione bisulfite and blood transfusions should be given to combat the prothrombin deficiency before the operation is begun.

DOSAGE AND FREQUENCY OF ADMINISTRATION

The purpose of dicumarol therapy is to produce a certain degree of prothrombin insufficiency. As with many other potent drugs, there is considerable variation in sensitivity to the drug among different patients. Absorption of the drug from the intestinal tract probably varies in different cases and there is some evidence that the effect may vary with the weight of the patient. The presence of fever, toxemia, and impaired nutrition also may influence the effect but there are still other unexplained differences in sensitivity. For these reasons it is necessary to individualize carefully the rate of administration of the drug for each patient.

We wish to emphasize again that dicumarol should not be used unless daily and consistently comparable prothrombin time tests are done, since without these it is impossible to be certain whether insufficient, adequate, or excessive and possibly dangerous effects have been produced. We believe that only the Quick prothrombin time test should be used for these determinations. Because of the importance of this test, some details regarding the technique and possible errors in comparative determinations should be mentioned.

The actual performance of the test is not difficult. Whole blood drawn from a vein is added to tenth-molar sodium oxalate in the proportion of 9:1. After a short period of centrifugation, 0.1 c.c. of plasma is placed in a small test tube and 0.1 c.c. of thromboplastin is added to the plasma. The tube with its contents is held in a constant temperature bath of 37.5° C. After a few moments 0.1 c.c. of fortieth-molar calcium chloride is added and at the exact instant when it is added, a stop clock (preferably operated with a foot pedal) is started. The tube is carefully agitated and then tilted at intervals to determine the moment at which a semisolid clot is formed; this is the end point and the clock is stopped. It is a sharp end point and can be duplicated by any technician who has had reasonable experience.

It is obvious from the description of the method that if there were no variables except prothrombin, the test could be considered a simple one. Unfortunately, the thromboplastin is distinctly a variable under certain conditions and the clotting time is dependent to a great extent on the activity of the thromboplastic substance. At the Mayo Clinic the thromboplastin which is used in the test is prepared from dried rabbit brain according to Quick's original method,[9, 10] that is, without previous extraction with acetone. We obtain a normal prothrombin time with this thromboplastin of seventeen to nineteen seconds. Some workers, however, follow Quick's modification of his earlier method.[11] In this modification he extracted the brain with acetone previous to the drying process. With this substance Quick obtained a normal prothrombin time of twelve to thirteen seconds and, with this, more active preparation times for various levels of prothrombin deficiency are all correspondingly

lower but by no means exactly six seconds lower for each level. Thromboplastins which give still different normal prothrombin times and therefore different and incomparable times for various levels of prothrombin deficiency have been used by other workers. Variations in results also may occur because two batches of thromboplastin which are made up in the same way and which give identical prothrombin times for normal plasma may not give identical times for a plasma with a moderate or marked prothrombin deficiency. As a result of our clinical experiences with dicumarol we found that prothrombin times of twenty-seven seconds, thirty-five seconds, and sixty seconds were indicative of certain important levels of prothrombin deficiency. However, such figures are meaningless to another worker using a different thromboplastin of different activity.

If normal plasma is diluted with prothrombin-free plasma so that 90 per cent, 80 per cent, and so forth down to 10 per cent solutions of normal plasma are obtained and prothrombin time tests are done on these various diluted samples, a curve can be plotted which will indicate prothrombin times for various percentage levels of prothrombin deficiency. An almost identical curve can be obtained if the dilution is made with physiologic solution of sodium chloride, except that it is more difficult to read end points in the higher dilutions. It is noteworthy that this curve is not a straight line. For example, the first few seconds' increase in the prothrombin time indicates a great decrease in the prothrombin percentage of normal but when the prothrombin deficiency becomes marked, many seconds' increase may mean a difference of only a few per cent in the concentration of prothrombin.

By plotting a dilution curve as indicated in the previous paragraph, any worker using a thromboplastin of unknown potency can determine a set of prothrombin times for that thromboplastic substance which indicate various percentages of prothrombin deficiency and if certain prothrombin percentages are considered important levels, he can easily determine their equivalents in prothrombin times.

Because of the variability of potency of thromboplastic substances, even when prepared by the same method, and because of the importance of having consistently comparable results from day to day when the test is used as a guide to dicumarol therapy, each new batch of thromboplastic substance should be checked against the one in use by one of two methods. Either only a new thromboplastin should be selected which gives the same results as the old, both with normal plasma and with a number of prothrombin deficient plasmas which are deficient to varying degrees, or a new dilution curve should be plotted for each new batch of thromboplastin. It may be advisable to check results on the same batch of thromboplastin if it is more than twenty-four hours old. As will be shown later, the important prothrombin times for patients receiving dicumarol are those for 10 per cent, 20 per cent, 30 per cent, and 100 per cent normal plasma. Determinations on other dilutions are

actually not necessary. It may be preferable from the standpoint of the clinician or surgeon who is supervising the administration of dicumarol that the reports be given in percentages of normal prothrombin rather than in seconds.

Our experience in the 1,000 cases in which dicumarol was used has been that with the thromboplastic substance which we have used, thrombosis or embolism almost certainly did not develop if the prothrombin time was greater than twenty-seven seconds, the time which corresponded to that of 30 per cent normal plasma, and that definite bleeding did not occur if the prothrombin time was less than sixty seconds, the time which corresponded to that of 10 per cent normal plasma. We have adopted arbitrarily thirty-five seconds, the time for 20 per cent normal plasma, as the key point in deciding about the dosage.

Dicumarol is effective when administered orally. A satisfactory preparation for parenteral administration has not been developed. We have endeavored to simplify the plan of administration as far as possible in order to keep the prothrombin level between 10 and 30 per cent of normal for each individual patient and we recommend the following plan of dosage: The entire amount of the drug for each day is given in a single dose. The first day 300 mg. are given and 200 mg. are given the second day. Two hundred milligrams are given on each succeeding day that the prothrombin is greater than 20 per cent of normal. If it is less than 20 per cent of normal, no dicumarol is given on that day. Exceptions are occasionally made as follows: If the prothrombin is dropping rapidly, but is still slightly greater than 20 per cent, no drug is given. If it is rising rapidly, but has not quite reached 20 per cent, a dose is given on that day. In the occasional patient who is found to be quite hypersensitive to the drug, it may be advisable to reduce some or all of the doses to 100 mg. In the occasional case of resistance, it may be advisable to increase them to 300 mg. For patients who have never had thrombosis or embolism and to whom the drug is given purely for prophylaxis, it may be advisable to omit the dose on the second day in order to be sure that the patient is not hypersensitive.

It must be re-emphasized that definite prothrombin deficiency does not develop immediately after the drug has been given. Effective levels are not reached for twenty-four to forty-eight hours and sometimes for a considerably longer time. If a rapid anticoagulant effect is desired, for example in a case of a large pulmonary embolism, administration of heparin and dicumarol should be started simultaneously. The prothrombin time may be used as a guide to the dicumarol effect alone if the blood is drawn for the test from three to four hours after an injection of heparin is given. Administration of heparin should be stopped as soon as the prothrombin has dropped to 20 per cent of normal. In dealing with patients who have had thrombophlebitis or a small pulmonary embolism we have rarely used heparin in addition to dicumarol and have almost never encountered a second episode of thrombosis or embolism during the one to three days which have elapsed

between the beginning of administration of dicumarol and the development of adequate prothrombin deficiency. Also it must be re-emphasized that the prothrombin deficiency may continue for from two to ten days after the last dose of dicumarol has been given. Daily prothrombin time tests should be continued until near normal levels of prothrombin have been reached.

We have maintained the prothrombin deficiency produced by dicumarol at levels between 10 and 30 per cent of normal for as long as three months among postoperative patients without untoward effect, without evidence of other impairment of hepatic function as measured by the ordinary tests, and with prompt return of prothrombin to normal within a few days after the administration of the drug was discontinued.

The prothrombin deficiency should be maintained until several days, preferably a week, after the patient has become ambulatory. The thrombosing tendency has almost certainly disappeared by that time. However, it must be emphasized that when the prothrombin has returned to normal there is no further protection against thrombosis.

CONTROL OF BLEEDING AND EXCESSIVE PROTHROMBIN DEFICIENCY

If, because of hemorrhage or abnormally high prothrombin times, it is advisable to lower the prothrombin time, this usually can be accomplished by the transfusion of 500 c.c. of fresh citrated blood (bank blood may be ineffective). It may be necessary to transfuse blood several times over a period of two or three days, since there is a tendency for the prothrombin time to increase again after two to six hours have elapsed. The effect of blood transfused for such a purpose apparently is due simply to a replacement of prothrombin, and blood which has been stored for more than twenty-four hours in the icebox may have lost much of its prothrombin.

In the original studies on dicumarol it was found that the administration of what were considered to be therapeutic doses of synthetic vitamin K did not inhibit the action of dicumarol or affect the hypoprothrombinemia which had been produced by dicumarol. However, it is now known that these doses were much too small. Overman, Stahmann, and Link[12] have pointed out that vitamin K inhibits the effect of dicumarol if given in large doses to rabbits. Shapiro, Redish, and Campbell[13] found that large amounts of synthetic vitamin K, given by mouth and intramuscularly to human beings, prevented the prolongation of prothrombin time following administration of dicumarol. By the intravenous administration of large doses of a special preparation of vitamin K_1 oxide, Davidson and MacDonald[14] were able in three of four cases to reverse to normal the prolonged prothrombin time induced by dicumarol. Lehmann[15] reported that the use of large doses of methylnaphthoquinone dihydrosulfate given orally with blood transfusions resulted in cessation of hemorrhage which had followed administration of dicumarol.

In the course of this study menadione bisulfite,* usually in a single dose of 64 mg., was administered intravenously to thirty-seven patients among whom an excessive deficiency of prothrombin had developed after administration of dicumarol. All but two patients responded satisfactorily to administration of menadione bisulfite. In thirty-two cases a marked and relatively rapid lowering of prothrombin time occurred, and in the other three, although the response was not great, the prothrombin time fell to within safe limits. No toxic or untoward reactions followed administration of menadione bisulfite.[16]

Bleeding which had occurred in three cases after administration of dicumarol, ceased after administration of menadione bisulfite in two cases and after administration of menadione bisulfite and a blood transfusion in the third case.

Patients may be encountered who are sensitive to dicumarol and whose prothrombin may fall to less than 10 per cent of normal after the first one or two doses or after subsequent doses. Ninety-three such patients (27 per cent) were encountered in a consecutive series of 340 who received dicumarol. Most of these were patients who had not had thrombosis or embolism. It is in this group that bleeding may occur, although it actually occurred in only three of these series of ninety-three. The safest procedure is to give a large dose (60 to 64 mg.) of menadione bisulfite intravenously to all patients whose prothrombin falls below 10 per cent of normal after administration of dicumarol and to use smaller doses of dicumarol thereafter. If bleeding of any serious or alarming degree occurs among patients who are receiving dicumarol, a large dose of menadione bisulfite should be given intravenously and a transfusion of fresh citrated blood should be given. Subsequent transfusions of blood should be given once or twice daily until the bleeding stops. The actual risk of bleeding is small among postoperative patients if the method of dosage and control mentioned previously is followed. It is particularly small among patients who have had some thrombotic or embolic episode (Table III).

COMMENT

When properly used, anticoagulant therapy with dicumarol and occasionally with heparin also for the first few days appears to us to be the most satisfactory method to date for the prevention of fatal postoperative pulmonary embolism. The risk of bleeding is minimal and if bleeding occurs it can be satisfactorily controlled. However, the prothrombin must be kept between 10 and 30 per cent of normal if the treatment is to be effective and safe. As opposed to ligation of one or both femoral or common iliac veins, anticoagulant therapy prevents venous thrombosis throughout the entire body. It is relatively simple,

*The preparation of menadione bisulfite was "hykinone" supplied through the courtesy of the Abbott Laboratories, North Chicago, Ill. Sixty-two and five-tenths per cent of hykinone is menadione (2-methyl-naphthoquinone).

does not involve further surgical procedures, and does not produce complete obstruction of veins containing thrombi which might undergo partial or complete involution. Therefore, it does not increase the hazard of chronic venous insufficiency of one or both legs with its disabling late complications.

Anticoagulant therapy seems to us particularly the preventive method of choice in cases of nonfatal postoperative pulmonary embolism or infarction in which the source of the embolus is not detectable clinically, in cases in which thrombosis or embolism has occurred prior to operation, and in those in which thrombosis or embolism has not occurred but in which it is thought that there is increased risk of these complications. Even in cases in which known venous thrombosis is present, anticoagulant therapy will prevent embolism because embolism develops only if a fresh thrombus develops. The old clots remain attached to the wall of the vein.

SUMMARY

Dicumarol has been given to 1,000 patients for the purpose of preventing postoperative venous thrombosis, pulmonary embolism, and thrombophlebitis. We have found it effective in preventing these complications in cases in which there has been nonfatal pulmonary embolism, thrombophlebitis or a history of previous thrombosis or embolism, and when the drug has been given prophylactically when no thrombosis or embolism has occurred. There is a small risk of bleeding. This can be further minimized by proper administration of the drug and rapid control of excessive prothrombin deficiency. Dicumarol should not be given unless daily and consistently comparable Quick prothrombin time tests are done. Consistently comparable prothrombin time tests depend on the use of thromboplastins of constant potency or on the checking of each new batch of thromboplastin with various dilutions of normal plasma. During the administration of dicumarol the prothrombin should be kept between 10 and 30 per cent of normal. Excessive prothrombin deficiency produced by dicumarol can almost always be controlled by the intravenous administration of large doses (60 to 64 mg.) of menadione bisulfite (synthetic vitamin K). If bleeding occurs as the result of excessive prothrombin deficiency, it can be controlled by transfusions of freshly drawn citrated blood and intravenous administration of large doses of menadione bisulfite.

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SURGERY OF DEEP VENOUS THROMBOSIS OF THE LOWER EXTREMITY

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ONCE thrombosis of the peripheral veins has developed, the objects of treatment are to limit propagation of the thrombus, to prevent pulmonary embolism, and to correct the local impairment of circulation. The method selected for obtaining these objects depends upon the type of thrombosis and the presence or absence of pulmonary embolism. At the present state of our knowledge, the only practical method in the great majority of cases is by surgical ligation of the appropriate vein above the level of thrombosis. Our purpose in this report is to present the experience with ninety-eight ligations of the major veins of the lower extremity for the treatment of deep vein thrombosis in eighty-four consecutive cases.

CLASSIFICATION

There are too many gaps in the fundamental knowledge of the etiology of venous thrombosis to allow a comprehensive classification. In general, however, cases involving the lower limb can be divided into two main groups: Acute thrombophlebitis and simple thrombosis (phlebothrombosis).

In acute thrombophlebitis, there is antecedent or concomitant inflammation of the vein wall. The clot forms on the intima, is firmly fixed, grows by accretion, and tends rapidly to fill the lumen completely along the involved segment. Acute iliofemoral thrombophlebitis is a typical example. The symptoms of this condition arise partly from inflammation and occlusion of a major vein and partly from reflex arterial spasm.[1, 2] Release of the vasospasm by means of lumbar sympathetic block (procaine) promptly relieves the symptoms of ischemia and limits extension of the thrombosis. With this form of treatment, recovery from the acute phase is usually complete within seven to ten days, and the ultimate results are most gratifying. Occasionally, pulmonary embolism follows detachment of a fresh thrombus which has formed above the inflamed segment of vein. In this event, ligation of the vein above the thrombus is the only safe method for preventing recurrent embolism.

Simple thrombosis (phlebothrombosis) most commonly begins in the small deep veins of the foot or leg. It differs from acute thrombophlebitis mainly by the absence of important inflammatory reaction in the early phase, by its tendency to propagate rapidly, and by the ease with which it becomes dislodged to cause pulmonary embolism.

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Between these two distinct types of venous thrombosis are many intermediate forms, which do not fall readily into any scheme of classification. Actually, most of the cases in this intermediate group undoubtedly begin as phlebothrombosis. Later a secondary inflammatory reaction may develop in and around the vein wall, so that the picture of acute thrombophlebitis is simulated. However, even at this stage the clot may not be firmly fixed to the endothelium and dislodgment remains a potential hazard. The existence of this intermediate group, plus the fact that embolism is occasionally seen in cases of typical acute thrombophlebitis, detracts greatly from the utility of the present system of classification. The eighty-four cases with which this presentation deals were all characterized by thrombosis of the type which begins in the lower leg and which shows a strong tendency to propagate. No attempt will be made to divide them into groups.

ETIOLOGY

The exact causes of intravascular clotting are still a mystery. Since this paper entails a purely clinical approach to one phase of venous thrombosis, it seems permissible to omit from discussion much that has been written about the etiology of the condition. From a clinical viewpoint the etiology of peripheral venous thrombosis is mainly a consideration of predisposing causes. In the eighty-four cases which are the basis of this report, some of the more important predisposing causes are shown in Fig. 1 and Table I.

Sex.—Of the eighty-four cases, fifty-five of the patients were men and twenty-nine were women. The incidence of the type of venous thrombosis for which surgical treatment is indicated is therefore considerably

TABLE I

PREDISPOSING DISEASE OR CONDITION AND INCIDENCE OF PULMONARY EMBOLISM IN 84 CASES OF DEEP VENOUS THROMBOSIS OF THE LOWER EXTREMITY

DISEASE OR CONDITION		NUMBER OF CASES	CASES WITH PULMONARY EMBOLISM
None (spontaneous)		20	11
Postoperative		20	10
Heart failure		12	7
Pulmonary tuberculosis		8	1
Pneumonia		5	3
Disease or injury of lower extremity		12	3
Fracture	4		
Cellulitis	3		
Gangrene	2		
Sprain	1		
Injected varicose vein	1		
Arthritis of knee	1		
Pregnancy		2	1
Severe burns		1	0
Prostatism		1	1
Meningitis		1	1
Cachexia		1	0
Influenza		1	1
Totals		84	39

higher in men than in women. This finding is in agreement with other reports.[3, 4] It is contrary to the experience with acute thrombophlebitis in which the ratio of women to men is reported as 3:2.[5]

Age.—Any type of peripheral venous thrombosis is very rare in the first two decades of life. The type with which we are dealing is not common until the fourth decade, and the majority of cases are after the fourth decade. About 70 per cent of the eighty-four cases involved patients over 40 years of age. This is in fairly close agreement with the findings of Allen, Linton, and Donaldson[3] who reported that 81 per cent of 202 patients with thrombo-embolic disease were over 40.

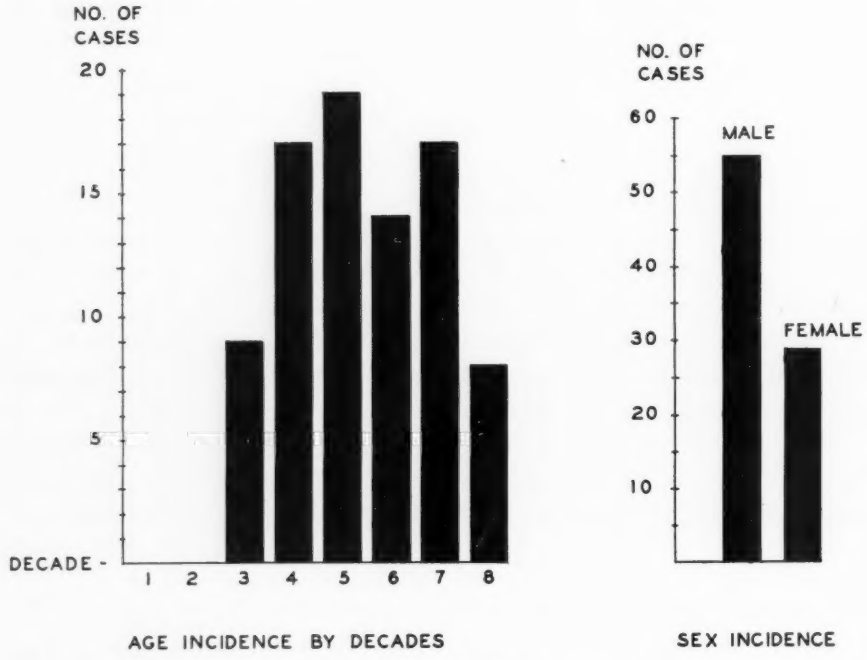

Fig. 1.—Predisposing factors in etiology of eighty-four cases of deep vein thrombosis.

Predisposing Diseases or Conditions.—The idea has been prevalent for years that thrombosis of the deep veins of the lower extremity is most common following pregnancy and abdominal operations. Hunter and his co-workers[6] demonstrated at necropsy, however, that in middle-aged and elderly patients the incidence of thrombosis of the deep veins of the leg is about equal in medical and surgical patients. Furthermore, Hampton and Castleman[7] found that in 370 autopsy cases of pulmonary embolism, 60 per cent were in medical cases and 40 per cent in surgical cases.

In the eighty-four cases of this series (Table I), only twenty were postoperative patients. Fifteen of the operations were on the abdomen, three were orthopedic operations, one was the removal of a brain tumor, and one was a lumbar sympathectomy for frostbite of the foot. This last

case is of particular interest because the thrombosis developed about eight days after a successful right lumbar sympathectomy. The thrombus was located in the lower part of the right femoral vein, as demonstrated by means of a venogram. Pulmonary embolism resulted in this case before the femoral vein was ligated.

There were also twenty cases in which thrombosis of the deep veins of the lower limb occurred spontaneously in individuals who were pursuing their usual routine of life. In four of these cases, thrombosis started in varicose veins and extended into the deep veins. In the remaining sixteen cases there was no history or evidence of previous disease of the veins, and the thrombus originated in the tibial veins. There was considerable variation in the types of activity in which the patients were engaged at the time of onset. Some of the activities included prolonged sitting in a cramped position, undressing in a Pullman berth, walking uphill while carrying a heavy load on the back, lifting a heavy weight, hiking to the point of fatigue, and prolonged standing at work. It is possible that there is one factor common to many of these cases, namely, distention and delayed emptying of the veins.

There were twelve cases of thrombosis in patients with heart failure. There was only one patient in this group less than 40 years old. The average age was 54 years. All of these patients had severe heart failure at the time of development of venous thrombosis. The factors which predispose to this complication in cardiac patients include venous stasis,[8] prolonged bed rest and free use of sedatives in treatment of the disease,[9] and possibly digitalization.[10] It is a curious fact that all of these factors prevail in children with heart failure, but thrombo-embolic phenomena are quite rare.[11]

Twelve of the eighty-four patients had thrombosis secondary to disease or injury of the lower extremity. Six of these resulted directly from injury to the bones or soft tissues of the extremity. Three followed cellulitis of the foot and leg. Two resulted from gangrene of the toes. The remaining case was one of severe arthritis of the knee. In all of these cases, with the possible exception of the last-mentioned, it is easy to conceive that the veins of the leg may have been directly involved by the disease or injury. In gangrene due to vascular diseases of the lower extremity, thrombosis of the deep veins is quite common. This is usually attributed to the slowing of the venous blood flow because of the diminished volume of arterial circulation. The prevalence of femoral vein thrombosis following thigh amputation has been emphasized by Veal,[12] who demonstrated a considerable reduction in the incidence of pulmonary embolism by high ligation of the femoral vein before amputation.

There were eight cases in patients with pulmonary tuberculosis who were on a regimen of strict bed rest. This group is of particular interest to us because of the slight attention that has been given to the vascular system in patients with this disease.

In the five cases of pneumonia, the patients were all seriously ill at the time that venous thrombosis developed. The remaining cases need no special comment.

It is obvious that in all of the eighty-four cases except the ones classed as "spontaneous," the conditions which predisposed to venous thrombosis were mainly ones in which prolonged rest in bed may have been the principal factor in the pathogenesis of the disease. We have omitted from analysis certain other conditions which are known[5, 8] to predispose to venous thrombosis, including obesity, infection, anemia, and malignant neoplasm.

SYMPTOMATOLOGY

In the eighty-four cases the symptom which first drew attention to the existence of thrombosis of the deep veins of the lower extremity was pain in the leg in sixty-one cases, evidence of pulmonary embolism in sixteen cases, and swelling of the leg in seven cases. The incidence of additional signs of the thrombosis is shown in Table II.

There was great variation in the type and degree of pain in the leg in the sixty-one cases in which it was a prominent symptom. Almost always the pain was located in the calf. In our experience, pain in the foot is a rare presenting symptom. In the patients who were well and active at the time of onset, the pain usually began suddenly and was sharp, persistent, and well localized in the calf. In bedridden patients the pain was variably described as constricting, aching, boring, or burning. Often the discomfort was intermittent, with or without reference to movement of the leg. On occasion, the pain was noticed for the first time when a patient who had been kept in bed was allowed to stand. In general, the pain was less severe and less well localized in the case of patients in bed. In many instances the patient noted that the pain extended in time from the calf into the popliteal region or thigh. The pain was almost never so severe as is seen in cases of acute iliofemoral thrombophlebitis.

The manifestations of pulmonary embolism as a presenting symptom will be discussed separately in a section to follow.

TABLE II

INCIDENCE OF VARIOUS SIGNS IN 84 CASES OF DEEP VENOUS THROMBOSIS OF THE LOWER EXTREMITY

SIGN	PRESENT		ABSENT	NOT RECORDED
	SIGNIFICANT*	NOT SIGNIFICANT		
Edema	72 (90%)	0	8	4
Calf tenderness	78 (96%)	0	3	3
Homans' sign	68 (92%)	0	6	10
Fever	12 (14%)	41	31	0
Tachycardia	18 (21%)	49	17	0

*The percentage figures in this column were obtained after excluding cases in which no record was made of the sign.

There were only seven cases in which edema of the foot or foot and leg was the first evidence noted of venous thrombosis. These were all

patients who were bedridden. In some of them the edema was erroneously ascribed at first to some other cause. We mention this fact only to emphasize the importance for the safety of the patient of remembering the possibility of venous thrombosis in any case of edema of the lower extremity. This is probably just as true whether or not there seems to be another obvious cause for the edema, such as heart failure or malnutrition. Although edema was the least common presenting symptom in the eighty-four cases, it was present at some time before surgical ligation of the affected veins in seventy-two cases. In four cases no record was made as to whether or not there was edema. We have included as instances of edema those cases in which the only evidence of its presence was enlargement of the calf, as detected by comparative measurements of both legs.

The most common sign of all was tenderness in some portion of the calf. This was elicited in seventy-eight of the eighty-one patients who were examined for it. A good deal of care is necessary in testing for calf tenderness. The patient's leg should be slightly flexed, so that the muscles are relaxed. Finger-point palpation should be made along the course of the deep veins, beginning at the plantar surface of the foot. Often the area of tenderness is quite small and well localized, but this is all the more significant.

Forcible dorsiflexion of the foot with the leg extended caused pain in the calf or popliteal area (Homans' sign) in sixty-eight cases. The results of this test were not recorded in ten cases. There were only six cases in which the test was negative. Allen, Linton, and Donaldson[3] reported this sign to be present in only 42 per cent of the cases in which the test was applied. Our experience, therefore, supports the contention of the author[13] who described the sign, that it may be expected to be found in a very high percentage of cases of tibial vein thrombosis. However, it should not be thought to be pathognomonic. It may be positive in a variety of other conditions, including peripheral neuritis, paralysis with foot drop, poliomyelitis, contusions without deep vein thrombosis, and cellulitis of the leg.

Fever and tachycardia, which are almost always present in acute iliofemoral thrombophlebitis, are not very helpful diagnostic signs in the type of venous thrombosis with which we are here concerned. These signs are usually lacking in the early stages of the thrombotic process, unless some other cause for fever and tachycardia is present. In the eight-four cases, fifty-three patients had fever at the time a diagnosis of venous thrombosis was made. However, in all but twelve of these patients the fever could be accounted for by the primary disease from which the patient was suffering or by pulmonary embolism. Sixty-seven patients had tachycardia, but on the same basis of analysis it was significant of venous thrombosis in only eighteen.

Venograms were made in only twenty-seven of the eighty-four cases. We have not used this type of study routinely nor do we advocate this.

The interpretation of venograms requires considerable experience with variations in normal venous patterns. This fact, plus the knowledge that a diagnosis of venous thrombosis can usually be made by means of simpler methods, limits the usefulness of the procedure. However, we have found that the venogram is an important aid in doubtful cases. In our experience a normal venogram usually excludes the diagnosis of thrombosis in the region studied.

PULMONARY EMBOLISM

In sixteen of this group of eighty-four cases, pulmonary embolism was the initial symptom that directed attention to the venous thrombosis, and in twenty-three additional cases pulmonary embolism preceded surgical ligation. This incidence is somewhat higher than was reported by Welch and Faxon,[14] who state that approximately one out of every three patients with deep phlebitis may be expected to have pulmonary embolism. However, it must be remembered that our figures deal only with cases in which ligation of a vein was performed and do not include a statistical study of pulmonary embolism in all cases of venous thrombosis.

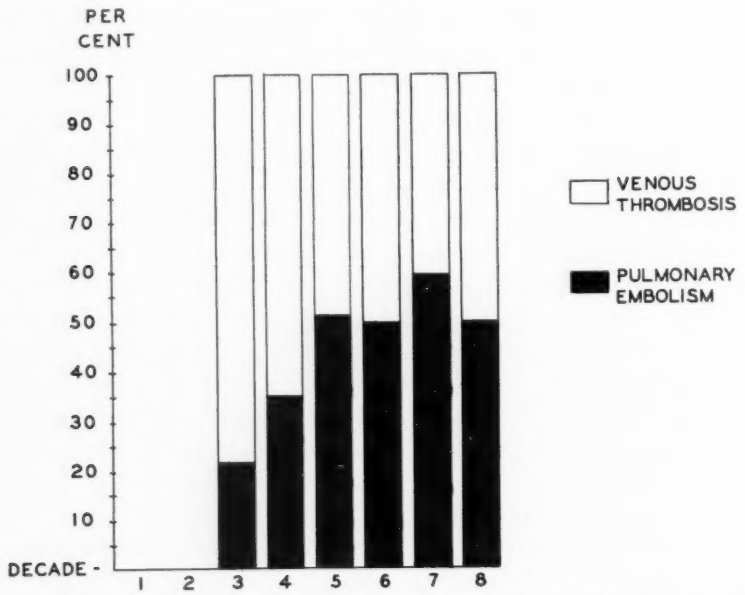

Fig. 2.—Incidence of pulmonary embolism by decades in eighty-four cases of deep vein thrombosis of lower limb.

Fig. 2 shows the incidence of pulmonary embolism by age in our cases. Of the patients in the third decade, 22 per cent had pulmonary embolism, and in the fourth decade, 35 per cent. Above the age of 40, slightly more than 50 per cent of the patients had pulmonary embolism, and there was remarkably little variation in the frequency of the complication in the different decades.

It has been our experience that cases of venous thrombosis are referred to the vascular surgeon in many stages of the thrombotic process. In

some cases the process is in an early phase, in others the disease has been present for weeks or even months before surgery is considered. The symptomatology varies correspondingly. Of prime importance in all cases is the prevention of pulmonary embolism. The surgeon, therefore, must answer the following question in each case: Is pulmonary embolism a potential danger, or has this case reached a "safe" period with respect to pulmonary embolism? We have already given the answer to the first part of this question. In all cases of venous thrombosis there is at some time danger of embolism. The latter part of the question is answered partially by the figures in Table III. This table shows the frequency of embolism in relation to the known duration of the thrombotic process. The sixteen cases in which pulmonary embolism occurred before the venous thrombosis was discovered are excluded from the table. The figures show that there is no "safe" period for all cases in the chronology of the disease up to four months.

In our discussion of the classification of deep venous thrombosis we have pointed out that the clinical picture in any case is not a perfectly reliable means for deciding about the likelihood of pulmonary embolism. Simple thrombosis of the deep veins of the calf, by propagation of the thrombus and secondary inflammatory reaction around the vein, may simulate acute iliofemoral thrombophlebitis, including massive edema. We have repeatedly observed at operation in such cases that the thrombus in the iliac veins does not necessarily become fixed to the intima for days or even weeks. We have also found that repeated

TABLE III

RELATION OF FREQUENCY OF PULMONARY EMBOLISM TO KNOWN DURATION OF VENOUS THROMBOSIS IN 68 CASES IN WHICH PULMONARY EMBOLISM WAS NOT THE FIRST MANIFESTATION

DURATION OF THROMBOSIS	TOTAL CASES	PATIENTS WITH EMBOLISM
Uncertain	5	3
1 Day	6	0
2 Days	6	1
3 Days	10	1
4 Days	4	0
5 Days	5	3
6 Days	1	0
7 Days	5	2
1 to 2 Weeks	9	2
2 to 3 Weeks	8	5
3 to 4 Weeks	4	3
5 to 6 Weeks	2	0
2 Months	3	2
4 Months	1	1

pulmonary embolism is common in these cases. Usually the emboli are small and arise from fresh clot engrafted on the older, organizing thrombus. We have recently observed at necropsy three examples of death from massive pulmonary embolism in cases of acute iliofemoral thrombophlebitis (phlegmasia alba dolens). In each instance the em-

bolus originated from a fresh thrombus engrafted on the older clot in the iliac vein. The vessels of the opposite extremity were entirely normal. We mention these points in order to temper a recent statement by Homans[15] to the effect that if pulmonary embolism occurs in cases of phlegmasia alba dolens, "one can be reasonably certain that it comes, not from the vein of the swollen limb but from the other, or innocent appearing leg." We quite agree, however, that when one lower extremity is the seat of venous thrombosis, the innocent-appearing limb should always be viewed with suspicion. This will be borne out in the discussion to follow on embolism after venous ligation.

One other question which deserves clarification concerns whether the circumstances under which venous thrombosis develops have any direct bearing on the frequency of pulmonary embolism. The incidence of this complication in the various predisposing diseases or conditions in our eighty-four cases is shown in Table I. We wish to emphasize particularly that the incidence was eleven out of twenty in the cases in which venous thrombosis occurred in active, apparently healthy individuals. This fact certainly demonstrates that a patient need not be bedridden to develop the type of venous thrombosis which leads to pulmonary embolism.

Pulmonary embolism which occurs after ligation of a major vein may originate from one of several sources. The most frequent source is undoubtedly from thrombosis in veins of the opposite lower extremity. It also may originate from a thrombus which forms in the ligated vein above the level of ligation, from veins in other parts of the body, or from thrombi in the right side of the heart. In nine of our eighty-four cases, the patient had pulmonary embolism after ligation of one or more veins. In each of these nine cases there had already been one or more episodes of pulmonary embolism before ligation. In five instances the embolus arose from the opposite, unoperated extremity, and in three the embolism was fatal. In four cases the embolus originated from a fresh thrombus above the point of ligation. In all of these the femoral vein had been ligated distal to the saphenous.

In forty-five cases the appropriate vein or veins were ligated as soon as venous thrombosis was recognized, and in none of these did pulmonary embolism develop.

OPERATIONS

The sites of ligation of veins in ninety-eight consecutive operations in eighty-four cases are shown in Table IV.* It is interesting to note that the veins of the right leg alone were involved in thirty-five cases, the left leg alone in thirty-three cases, and both legs in sixteen cases. Thus, the frequency of thrombosis was about equal in the right and left lower

*In this paper we have used the term "ligation" loosely. Actually, in almost all cases, the procedure has consisted of opening the vein for inspection, ligating above and below the opening, and dividing the vein between these ligatures.

extremity. This experience is somewhat at variance with the statistical report of Barker and his co-workers[16] to the effect that thrombophlebitis is about twice as common in the left lower extremity as in the right. Of great importance is the fact that in our patients about one-fifth had venous thrombosis in both lower extremities.

TABLE IV

SITES OF LIGATION FOR TREATMENT OF 84 CASES OF THROMBOSIS OF DEEP VEINS OF LOWER EXTREMITY

SITES OF LIGATION	NUMBER OF CASES
Right femoral	20
Right femoral (thrombectomy)	1
Left femoral	19
Left femoral (thrombectomy)	3
Right external iliac	4
Left external iliac	1
Right common iliac	7
Right common iliac (thrombectomy)	3
Left common iliac	7
Left common iliac (thrombectomy)	3
Inferior vena cava	2
Multiple operations	
Both femorals (simultaneous)	6
Right common iliac and left femoral (simultaneous)	1
Both common iliacs (separate)	3
Left common iliac (thrombectomy) and inferior vena cava (thrombectomy)	2
Left external iliac and inferior vena cava	1
Right femoral and inferior vena cava	1
Total cases	84 (Total ligations, 98)

As yet the operative treatment of venous thrombosis is not completely standardized. In all reports there is considerable variation of opinion as to the level at which ligation should be done. We have attempted to follow one rule: Ligate the affected vein above the level of the thrombus in a normal segment of vein just distal to a main tributary. By this means the entire pathologic process is trapped below the point of ligation. The main tributary assures an adequate flow of blood to diminish the chance of development of a fresh thrombus. This also excludes a blind end of vein in which a thrombus may form. There is great danger of recurrent thrombosis when ligation is performed through a diseased segment of vein, although the clot may have been removed or may not have extended to this level. We have had four cases of recurrent pulmonary embolism following ligation of the femoral vein through a diseased segment. We have had other cases in which a thrombus formed above the point of ligation through a diseased segment and extended into the inferior vena cava, making a secondary and more hazardous operation necessary.

In cases in which, on exploration, a clot is found at the level of operation, the course to be followed depends upon the age of the thrombus and the condition of the vein wall. A fresh clot is blue, elastic, resilient,

and unattached to the intima. This type of clot can be removed safely, providing that the vein wall shows no sign of inflammation. When the vein wall is definitely inflammed, regardless of the appearance of the clot, it is safer to go higher and ligate the vein where it appears normal. When the clot is old and organizing, it is brownish and friable. Thrombectomy is then dangerous because of the likelihood of dislodging fragments of the clot.

Ordinarily, poor general condition of a patient is a deciding factor against any form of surgery. However, in cases of pulmonary embolism from venous thrombosis, even the patient who appears hopelessly ill is a candidate for ligation of the affected vein. Many of our patients were operated upon when they were extremely ill as the result of multiple pulmonary emboli. The danger of another episode of embolism seemed greater than the strain of operation. There were no deaths attributable directly to the operation.

In each of forty-five cases, including multiple operations, one femoral vein was ligated. In four of these a thrombus was removed at the time of operation. In six additional patients both femoral veins were ligated at the same operation. In almost every instance the point of ligation was just distal to the entrance of the saphenous vein into the femoral. In none of these cases have we seen any evidence of subsequent thrombosis of the saphenous vein. The femoral vein was explored only in those cases in which it was believed from the clinical picture that the thrombus had not extended above the inguinal ligament. In a few cases the femoral vein was explored and found to be inflamed. The process therefore was older than we had anticipated. In such cases the first incision was closed and the common iliac vein was ligated.

The external iliac vein was ligated in only six cases. This vein is very accessible, but because of the problem of collateral circulation,[15] ligation at this level is less desirable than at the common iliac.

Counting the cases in which multiple operations were done, a common iliac vein was ligated twenty-nine times. Ligation was done fourteen times on the right side, fifteen times on the left side. In eight instances a thrombectomy was performed at the same time. All of these operations were done by means of an extraperitoneal approach to the veins. We have found that the left common iliac vein can almost always be exposed satisfactorily for proper exploration of the lumen of the vein preceding ligation.

In six cases it was necessary to ligate the inferior vena cava; four times because of thrombosis in both iliac veins, and twice because of extension of inflammation from the left common iliac vein to the wall of the vena cava. Pulmonary embolism had occurred before ligation in all of these cases. In five instances the thrombosis originated in the tibial veins. The sixth case was one of typical iliofemoral thrombophlebitis which had seemed to be responding well to treatment by means of re-

peated infiltration of the lumbar sympathetic ganglia with procaine solution. After all evidence of the inflammatory phase of the disease had subsided, the patient developed pulmonary embolism. At operation it was found that the lower part of the inferior vena cava was inflamed and that a clot projected into its lumen from the left common iliac vein. There was no involvement of the veins of the other lower extremity.

In Table IV the types of multiple operations are listed separately. It is to be understood that in each instance the multiple operation was necessary because of obvious signs of pathology in the veins ligated. About one in every five of our patients showed positive evidence of bilateral involvement. There may have been others in which the disease was not recognized to be bilateral. We are in agreement with the thought[3] that bilateral ligation probably should be done more frequently.

RESULTS OF OPERATIVE THERAPY

As stated earlier, the objects of treatment of thrombosis of the deep veins of the lower extremity are to prevent pulmonary embolism, to limit propagation of the thrombus, and to correct the local impairment of circulation. Evaluation of the results of operative therapy must be made in the light of these objects.

There is no question that ligation diminishes the likelihood of pulmonary embolism. In forty-five cases in which pulmonary embolism had not preceded ligation, there was no instance of embolism subsequent to ligation. In view of the fact that Welch and Faxon[14] estimate that the chances of developing pulmonary embolism in the type of venous thrombosis under discussion are about one out of three, this is indeed a significant achievement. Of thirty-nine cases in which pulmonary embolism occurred before ligation, nine patients also had embolism after ligation. In the light of the experience gained in the management of these cases, most of the postligation embolisms could have been prevented. In five instances the source of embolism was the opposite, unligated side. In the other four the origin of the embolus was in the femoral vein above the point of ligation, and in three of these the vein showed definite inflammation at and above the point of ligation. Therefore, in eight of the nine cases of postligation embolism, the recurrent embolism was the result of inadequate surgical treatment rather than a fault of the principle of treatment.

Ligation of a deep vein at a normal segment above the level of thrombosis will unquestionably trap the clot already formed and will prevent the formation of a thrombus above the point of ligation in almost every case. Thus, only one out of eighty-four patients developed thrombosis above the level of ligation when these principles were observed. In addition, it has been our impression that after ligation there is less tendency of the thrombus to extend in the veins below the level of ligation than when the disease is allowed to pursue a natural course. There-

fore, surgical treatment effects a saving in patent venous channels which will be available for the development of collateral circulation.

Ligation cannot be expected to remove the venous obstruction that has already developed. In many instances, it temporarily increases the obstruction. The degree to which this local impairment of circulation will be corrected depends upon the adequacy of the collateral circulation. This in turn depends upon the extent of the thrombosis and the number and size of veins available as collateral channels. The point of ligation also affects the efficiency of the collateral circulation. We have found that patients in whom the inferior vena cava or common iliac vein is ligated usually develop a more complete collateral circulation than those in whom the external iliac or femoral vein is ligated.

The functional restoration of the involved extremity after ligation is excellent. Pain, which is a common complaint before ligation, quickly disappears. In some cases the relief of pain is dramatic. Vasospasm, if present, is usually abolished very promptly. However, in this series, ligation provoked arterial spasm in three cases, which are to be the subject of a separate report.[17] Edema, a very frequent finding before operation, is sometimes temporarily increased following ligation. The edema usually subsides after a few days of rest and elevation of the extremity. It has generally been our policy to have the patient wear an elastic stocking when activity is resumed. This is worn until edema no longer develops as a result of activity. It has been of special interest to us to follow the progress of the cases in which the inferior vena cava was ligated. The complete restoration of function in these cases that were seemingly hopeless at the time of operation has been most gratifying.

In this series of eighty-four cases there were seven deaths. Three resulted from recurrent pulmonary embolism, originating in the unoperated extremity. Four patients died from the combination of their original diseases and preoperative multiple pulmonary embolism.

SUMMARY AND CONCLUSIONS

1. We have presented data on eighty-four cases of thrombosis of the deep veins of the lower extremity treated by ligation of the affected veins.

2. A total of ninety-eight ligations were performed. The sites of ligation were the inferior vena cava (six times), common iliac vein (twenty-nine times), external iliac vein (six times), and femoral vein (fifty-seven times).

3. In forty-five cases in which ligation was performed before the development of pulmonary embolism, there were no instances of this complication. In thirty-nine cases in which the operation was done after at least one episode of pulmonary embolism, there were nine cases of postligation embolism.

4. There were no deaths as a result of operation.

5. Ligation therapy effectively limits the propagation of a thrombus, prevents pulmonary embolism, and permits more rapid and more complete restoration of function of the involved extremity.

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THE SURGICAL THERAPY OF THROMBOSIS OF THE DEEP VEINS OF THE LOWER EXTREMITIES

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THE most important achievement of the past few years in relation to pulmonary embolism is the growing realization that embolism occurs nearly always as a consequence of venous thrombosis in the large deep veins distal to the inferior vena cava. After Murray and Best[1] reported favorably on the administration of heparin to forestall the occurrence of thrombosis or embolism, this therapy acquired widespread popularity, but the expense and considerable annoyance to the patient incident to its administration led to its partial or complete abandonment among the advocates[2, 3] of dicoumarin, which is cheap and given by mouth. Simultaneously, with the acceptance of these modes of therapy, a surgical approach to the problem came to the fore, largely owing to the observations of Homans,[4] who among American surgeons at least appears to be the first to have deliberately ligated the common femoral vein to forestall the discharge of an embolus. There followed a number of contributions[5-9] from various clinics on the virtues of the more or less routine adaptation of Homans' maneuver and these clinics have, to date, persisted in this surgical approach in preference to the use of either heparin or dicoumarin.

Statistical data on the prophylactic value of any and all of these methods are of dubious validity because of the impossibility of assessing the incidence of venous thrombosis in the patients studied, since it is now quite clear from autopsy evidence that a large percentage of people have this condition without subjective or objective evidence of its presence. Moreover, an unfortunately high percentage of infarctions and fatal embolisms occur in the absence of all signs of the thrombosis responsible for them. What remains as a basis for selection of one of the three methods of therapy is perhaps the clinical impression of the efficiency of these agents once the thrombosis is known to exist. Those who prefer the surgical approach do so usually because of the dangers or demonstrated futility of heparin or dicoumarin in individual instances. For our purpose it will suffice to refer to two recent reports on dicoumarin. Evans[3] recommends it as the method of choice in spite of the fact that of fifty-five patients to whom it was given, eight developed postoperative hemorrhage sufficient to cause death in two and in spite of the fact that two patients discharged emboli (one of which was fatal), one during the administration of dicoumarin and one after the administration was stopped. Barker and co-workers[2] likewise urge the

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adoption of dicoumarin even though hemorrhage occurred in some 10 per cent of the cases in which it was given. That similar experiences have occurred from the use of heparin can be testified to by those who have given it with a critical eye to its effectiveness as well as its safety. One need not here stress the considerable energy and constant watchfulness necessary for effective maintenance of a delayed coagulation time, as well as the frequent failure to achieve the desirable level with uniformity because of unpredictable responses to predetermined dosage.

In making a choice between these drugs on the one hand and surgical treatment on the other, it is appropriate at this point to discuss also the shortcomings of surgical treatment. These have been discussed by Homans,[10] Fine, Frank, and Starr,[9] and others. The fluidity of the present status of surgical therapy derives from them and they can best be illustrated by pointing up the lines upon which those who prefer this method agree and those upon which they differ.

Quiet Venous Thrombosis (Phlebothrombosis) Versus Thrombophlebitis.—The distinction implied in this heading[10] is stressed with some emphasis by Ochsner and DeBakey[11] and concurred in by Homans,[10] who states that thrombophlebitis involving the femoro-iliac system is a fully obstructing type of thrombosis accompanied by outspoken perivascular inflammation and swollen lymph nodes, in which the thrombus is so firmly attached that embolism need not be feared. "The greater the swelling and discomfort the less the danger that a soft detachable mass exists." "And if . . . embolism actually occurs, one can be reasonably certain that it comes not from the vein of the swollen limb but from the other or innocent appearing leg." In quiet venous thrombosis, according to Homans, a soft nonobstructing detachable clot exists and perivascular inflammation is not an outspoken feature; therefore the danger of embolism is great. In the strict pathologic sense such a distinction has validity only in that there are gradations from case to case in the amount of adherent thrombus, soft loose clot, and perivascular inflammation. It is our opinion that from the clinical viewpoint this distinction is dangerous if it is relied upon as a basis for interference or noninterference for the prevention of embolism. For our experience convinces us that one cannot tell in any given case whether or not a soft clot is present regardless of the estimated degree of thrombosis present. That loose clot can be present in the full blown clinical condition of phlegmasia alba dolens is illustrated by the following recent cases:

CASE REPORTS

CASE 1.—I. R., a woman, aged 35 years, developed an ischio rectal abscess two weeks following discharge from the hospital after a cholecystectomy. Two weeks after drainage of the abscess she complained of severe pain in the left calf which was swollen and tender. Three hours later she developed tachycardia, substernal distress, and pain in the right posterior chest aggravated by breathing or coughing. Four hours later she showed massive edema and moderate cyanosis of the entire leg, a tense bulging tender calf area, and tenderness along the entire femoral vein, with evidence of inflammatory swelling in the femoral glands. Immediate explora-

tion of the left pelvis extraperitoneally showed marked acute perivascular inflammation, acute lymphadenitis, spasm of the iliac artery, and a tense bulging iliac vein, from which a long soft unattached clot was sucked out. The right common femoral vein was ligated also, but no inflammatory reaction was seen in this region. Three weeks later the right ankle was slightly edematous; otherwise both legs were normal, though cool, and with a slight cyanotic tinge of all the toes.

It may be argued that the embolus came from the right lower leg veins and not from the left iliac vein. But the proved presence of a long soft loose clot in the left iliac is impressive evidence that acute thrombophlebitis with a "fully obstructed venous system" cannot be dismissed as free from the danger of embolism and that the safest course is to assume nothing as to the precise nature of the clot or thrombus and its embolic potentialities until it is exposed to view.

CASE 2.—A 28-year-old woman who had been gotten out of bed on the third day after cesarean section complained of pain in the left thigh. The next day examination showed a small area of tenderness and induration in a tributary of the internal saphenous vein. There was no fever. Two days later the entire leg was found swollen from ankle to groin. The leg was cyanotic, especially when dependent. Tenderness was present in the calf, along the femoral vein, and in the groin. Exploration revealed plastic exudate about the femoral sheath, the femoral artery was constricted, and the femoral veins, both deep and superficial, were distended with thrombus. The femoral lymph glands were swollen. A long soft nonadherent clot was aspirated from the iliac vein through an incision in the common femoral. Older thrombus was present distal to the opening in the vein. An uneventful convalescence followed.

CASE 3.—S. K., a 36-year-old man, thirteen days after an abdominoperineal resection, developed pain and swelling in the left calf. The next day the entire leg up to the groin was greatly swollen, the lower leg was tense. Distended superficial veins, a positive Homans' sign, and tenderness in the groin and along the femoral vein were present. The vein was exposed and a large soft clot extending proximally well up into the common iliac was sucked out and the vein divided. There was considerable perivascular inflammatory reaction and the femoral lymph nodes were edematous and hyperemic. Slow but steady resolution took place so that one month thereafter all signs of the process had vanished.

The foregoing three examples of femoro-iliac thrombosis could not be distinguished from classical so-called milk leg. There is little doubt that the size of the soft clot in all these patients, if fully detached, could have caused fatal embolism. There is also little doubt that if the clot had not become loosened it would have been converted in time to an adherent thrombus. Hence it would be more correct in our view to say that the longer the patient has had femoro-iliac thrombosis, the less the likelihood of a fatal embolism. But if the condition is detected early enough one cannot say that the clot is or is not adherent. Accordingly, we find it expedient, except in long-standing cases, to explore every patient without making a distinction which may work to the greater deterriment of the patient than would exploration of the vein.

Unilateral or Bilateral Ligation.—The literature is now replete with pathologic data on the astonishing frequency with which the process

of thrombophlebitis of the lower extremities occurs bilaterally. The more thoroughgoing the investigation is of the deep veins, the higher the frequency, so that there is little doubt that at least one-half of all patients with the disease have it on both sides. Since the disease is commonly devoid of all signs of its presence, the practice of ligation on both sides, when only one side is obviously involved or when infarction has occurred, irrespective of the apparent extent of involvement of either side, is the safest prophylactic measure against embolism.

Venography.—In a previous statement of the problem[9] we urged venography on two grounds: (a) to determine the presence of the disease and (b) to determine the proximal extension of the process in order to define the level of attack upon the clot. We have with increasing experience come to find the value of venography much more limited than we had believed, for the following reasons:

1. The clinical signs of the disease were sometimes present in the absence of venographic evidence.

2. Spastic irregularity or spastic obliteration may occur and be impossible to distinguish from organic occlusion.

3. When one side is clearly involved and the other side by venography appears not to be, the avoidance of ligation of the uninvolved side has not infrequently been followed by the necessity of doing the ligation on this side because of the subsequent development of unmistakable evidence of the disease by venography or signs and symptoms or both. Meanwhile, the avoidance of the ligation may have allowed infarction to take place by embolism from that side.

The Level of Surgical Attack.—Embolism occasionally occurs even when bilateral femoral ligation is performed. This is not difficult to understand if a clot present above this level is overlooked, incompletely removed, or forms after ligation. The likelihood of this occurrence is minimal when the process on both sides is confined to the veins below the knee or well below the common femoral. It is maximal when the clot is not entirely removed or overlooked above the site of ligation or in excessively thrombophilic individuals who continue setting up new foci proximally. An example of the extraordinarily bizarre possibilities is illustrated in Case 4.

CASE 4.—N. W., aged 32 years, was said to have suffered from grippe and sinusitis complicated by an atypical rheumatic syndrome for a period of five months, during which he was alternately in and out of bed. He then began coughing and showed signs in both lower lobes suggestive of bronchopneumonia. For several weeks before admission to the hospital he coughed up streaks of blood and for one week bright red blood in small amounts frequently. During this week he had stabbing pain on respiration along the right costal margin and began having pain in the left leg. When seen by one of us he showed little local disturbance in this leg except for tenderness along the femoral vein and in the calf, and slight edema of the

whole leg, chiefly below the knee. The right leg was entirely devoid of signs or symptoms. Under spinal anesthesia the left external iliac vein was exposed. Perivascular inflammation and swollen lymph nodes were present. The vein was distended and tense and a large soft clot was extracted from the distal and proximal extensions of this vein. When the vein was entirely empty and free flow from above was obtained by suction, it was ligated and divided between ligatures. The right common femoral vein was then exposed. No inflammation was seen around this vein or in the femoral glands and the vein was free of clot. It was ligated in continuity and the patient returned to bed. One hour later the patient was in shock and evidence of massive embolism was present. Eight hours later death occurred and autopsy disclosed massive pulmonary embolism. The embolus had become detached from an isolated area of thrombosis confined to the proximal few inches of the right common iliac vein with no involvement of the deep venous system distal to this segment. The fractured end of the clot fitted into that of the thrombus still in situ. On the left side a soft clot was found in the lower left leg in the popliteal vein.

The probability of identifying this thrombus by venography is remote. Even with knowledge of its presence nothing less than ligation of the vena cava would have prevented death. But if we are to do anything less than ligation of the vena cava at the bifurcation whenever ligation is to be done at all, much more experience than is at present available must be had on the consequences of this procedure. Persistent edema of the extremities and occasional shock due to sudden increase in tension of the distal venous system with consequent local loss of plasma into the tissues may prove to be not uncommon complications of this procedure. Such plasma loss may be expected to be only temporary since the caval block will be by-passed effectively, mainly via the intraspinal venous sinuses.

Until such experience is extensive enough, the appropriate attitude toward the problem will be to confine ligation to both common femorals above the profunda, to one common iliac and one femoral, or, if both common iliacs require ligation, to do the simpler procedure, that is, vena cava ligation.

What are the indications for choosing among these alternatives? While the approach to the iliac is certainly more of a surgical undertaking than that to the femoral, it is well borne by even very sick patients. Both common iliac vessels can be exposed through the same incision.[11] There are sufficient cases in which the operator, having cleared the iliac as well as possible through an opening in the femoral vein, cannot feel satisfied that he has not left some clot. It is also plain that even complete evacuation of all clot, if mixed with some adherent thrombus, must leave damaged intima which permits the reformation of both thrombus and clot. It is no longer sufficient, therefore, to approach involvement of the iliac vein by femoral phlebotomy. A direct approach is essential. An index to the necessity of direct exposure of the iliacs is any or all of the signs indicating their involvement, which are as follows: (1) swelling of the thigh, mild, moderate, or severe; (2) pain in the groin and tenderness in the groin or along the upper part of the

femoral vein; (3) swelling of the femoral lymph nodes; (4) cyanosis of the thigh; (5) dilatation of the superficial veins of the thigh. But even in the absence of all these signs and symptoms, one may find involvement of the iliacs when the femoral vein is exposed. If, on approaching this vein, there is perivenous inflammatory reaction, involvement of the iliac is likely and a shift in surgical approach should be undertaken, if one is not clearly beyond the clot at the site of phlebotomy.

Ligation of the common femoral vein is the method of choice in the presence of signs indicating involvement limited to the deep veins below the knee or if pulmonary embolism has occurred, even in the absence of all signs of thrombophlebitis.

In a previous communication[9] it was pointed out that fatal embolism has occurred from thrombosis of the vena profunda femoris when it has been spared by ligation of the superficial femoral vein. We persist in this view regardless of how innocuous the profunda may seem, for only a short segment of it can be visualized. The greater likelihood of edema after blocking the common femoral rather than the superficial femoral is a small consideration in view of the greater safety of the former.

While edema, cyanosis, and pain may persist or even increase after iliac or femoral vein ligation, it is impossible to determine how persistent these phenomena might have been had no ligation been done, for the operation may be undertaken without knowing whether the disease is in the florescent or deflorescent phase in a given individual. Our experience supports the statement of Homans[10] that edema due to blocking flow by ligation is seldom as pronounced when the iliac is interrupted as when the common femoral is interrupted. The postligation edema, whatever its cause, is of only minor consequence in the considertion of the best level, that is, the safest level for ligation. On the score of safety we refer primarily to the certainty of blocking the potential embolus and secondarily to the risk of the procedure itself. Many hundreds of ligations have now been done, including the external and common iliac veins and the vena cava just above its bifurcation. Those familiar with the techniques involved can testify to the relative innocuousness of these procedures, at least compared to the dangers such procedures are intended to forestall. In our own experience we cannot account for a single fatality clearly attributable to the procedure itself.

As to the effectiveness of these procedures in preventing embolism we will, along with others, readily admit the occasional occurrence of infarction and, rarely, of fatal embolism following operation. Almost always this has occurred because the ligation was unilateral or at too low a level and occasionally after what appeared to be a quite adequate level. It is for this reason that vena caval ligation may come to occupy a significant place in the prophylaxis of embolism.

Age.—It is quite clear that no age is exempt from deep thrombophlebitis of the lower extremities and that while it is rare in patients

under the age of 20, it is sufficiently common under the age of 40 to leave one without assurance that an embolus will not follow phlebitis in a young adult

No adult who is confined to bed for any reason, whether for a medical or surgical condition, may be regarded immune to the disease. While it is commoner in elderly patients, for example, those with prostatic disease; in people with varicose veins, especially those who have already had a previous deep phlebitis; in elderly patients with coronary disease; in those with carcinoma of the tail of the pancreas; and after a low-thigh amputation, there is no guide which permits relaxation from close observation for the presence of phlebitis, if fatal embolism is to be avoided.

From the foregoing discussion one is aware that the present status of surgical therapy is still confused and leaves much to be solved in attaining the ideal prophylaxis against embolism. Indeed, even when surgical therapy is intelligently applied, occasions will arise when heparin or dicoumarin may be correctly employed in addition, unless perhaps the vena cava itself has been ligated. This will be the case if infarction continues and no other surgical procedure is indicated or deemed wise. But these anticoagulants should even then be used with a clear understanding of their limitations, for it is not to be expected that every patient will be assured of recovery from threatened embolism if all three methods are employed.

Since the occurrence of deep thrombophlebitis is so clearly related to inactivity and recumbency, the prophylaxis against the development of this disease has included the practice of early, active, and continued motion in bed, and as early rising as possible for surgical and non-surgical patients. For the past year we have gotten most patients out of bed within a day or two after operation, not excepting such patients as have had gastrectomy or abdominoperineal resection. We have no less than five patients in this series who developed thrombophlebitis nevertheless. It is perhaps appropriate here to remark that being up in a chair and walking occasionally during the first few postoperative days is not equivalent to early active motion of the extremities.

SUMMARY AND CONCLUSIONS

1. Heparin and dicoumarin are useful but not thoroughly dependable agents for the prophylaxis of pulmonary embolism. Their use is furthermore complicated by the occurrence of hemorrhage in wounds and elsewhere, which has occasionally proved fatal.

2. The surgical prophylaxis of pulmonary embolism is the procedure of choice among those who prefer a more direct and immediately applicable method for blocking the discharge of an embolus. The risks of ligation of the common femoral, the iliacs, and possibly also the vena cava are minimal and are accompanied by little postoperative dis-

turbance except for transitory increase in edema in occasional instances. This increase in edema is less likely to occur when the common iliac vein is ligated.

3. The selection of the level of ligation is made on the basis of the evidence of the extent of involvement: (a) the common femoral vein is ligated when thrombophlebitis is limited to the veins below the knee or when pulmonary embolism has occurred in the absence of all signs of involvement; (b) the common iliac is ligated when thrombophlebitis involves the common femoral, external, or common iliac veins; (c) the vena cava is ligated when the indications are that both common iliacs require ligation.

4. Since the frequency of bilateral involvement is high, bilateral vein ligation is generally indicated.

5. The occurrence of spastic narrowing or obliteration of venous channels limits the diagnostic usefulness of venography.

6. The distinction between quiet venous thrombosis and full-blown thrombophlebitis, that is, phlegmasia alba dolens or milk leg, is not a dependable means of deciding when a clot is detachable and when it is not. Therefore, exploration of most cases of so-called milk leg is advisable.

7. Early mobilization after operation does not provide full security against the development of thrombophlebitis.

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INTRAVENOUS CLOTTING

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INTRAVENOUS clotting is of great significance because of its complications and its sequelae. Whereas previously all forms of intravenous thromboses were considered as being similar, it is our conviction that from etiologic, clinical, prognostic, and therapeutic standpoints, it is necessary to distinguish between two major types, thrombophlebitis and phlebothrombosis.[82-85, 96] The clotting in thrombophlebitis is the result of injury to the vascular endothelium from mechanical trauma, chemical injury, or bacterial invasion, whereas in phlebothrombosis, the intravascular thrombus formation is due to alterations in the cellular and fluid constituents of blood, which increase the clotting tendency, and to venous stasis. The clinical manifestations of the two types of intravenous clotting are entirely different. In thrombophlebitis, the symptoms are marked, whereas in phlebothrombosis there are few, if any, clinical manifestations. The prognostic significance of this differentiation lies in the fact that in thrombophlebitis, unless there is suppuration which is rare, the clot is firmly adhered to the vein wall and therefore is not likely to become detached and result in embolism. Because of the associated inflammatory process, it is usually accompanied by profound arterial spasm resulting in edema which may persist and cause prolonged disability. On the other hand, the coagulum in phlebothrombosis is loosely attached to the vein wall and can be detached easily, resulting in embolism. The therapy of the two conditions is also different. Because the clinical manifestations in phlebothrombosis are due to associated vasospasm, the relief of vasospasm usually results in prompt relief of symptoms and subsidence of the lesion. On the other hand, in phlebothrombosis, either thrombectomy or the ligation of the vein above the thrombus is imperative in order to prevent a possible fatality from pulmonary embolism.

As a result of any trauma, changes may occur in the blood constituents which favor clotting. This is undoubtedly a protective mechanism and at times is necessary in order to prevent excessive hemorrhage. Unfortunately in many instances, the increased coagulability of the blood is undesirable and is the predisposing factor in the production of intravenous clotting. The trauma may be accidental, the result of an operation or delivery, or may follow the invasion of tissue by microorganisms or neoplastic tumors. The principal precipitating factor in intravenous clotting and the one which is of importance in the determination of the site of the involvement is circulatory retardation, because as a result of slowing of the blood stream in an individual in

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whom there is an increased clotting tendency, intravenous thrombosis is likely to occur. Other predisposing factors are cardiovascular disease, advancing age, seasonal variation, constitutional diathesis, obesity, debility, varicosities, excessive smoking, anemia, and foci of infection. Ophüls and Dobson[94] stated that cardiac disease was present in 52 per cent of their cases of thrombosis and embolism, and Putnoky and Farkas[100] found that approximately 90 per cent of their ninety-one patients with pulmonary embolism had cardiovascular disease at the time of the fatal seizure. Burke[18] states that of a total of 648 cases of intravascular clotting, 444 were associated with cardiac disease. His findings emphasize further the importance of cardiovascular disease in the development of thrombosis because there were 218 patients who developed thrombosis after escaping it following a previous operation. Intravenous clotting is particularly likely to occur in older persons, probably because of circulatory retardation subsequent to cardiac weakness and also to degenerative changes within the vascular tree, both of which predispose to intravenous clotting. Ewald[27] states that venous thrombosis is exceptional in young persons and occurs only when there is a circulatory disturbance. According to Stieh[118] 83 per cent of his patients who had embolism were past 40 years of age, 66⅔ per cent past 60, and 20 per cent past 70. Allen, Linton, and Donaldson[2] observed 202 cases in which femoral interruption was necessary for intravenous clotting; 81 per cent of the patients were past 40 years of age, and only 19 per cent younger than 40. Fifty per cent were between the ages of 50 and 70.

There is considerable variation in the incidence of intravenous clotting according to the seasons and according to the locality.[84] Generally, intravenous clotting occurs more frequently during the spring and winter months than during the summer months, and the incidence is definitely higher in the northern clinics than in the southern ones. The average incidence in the northern states is 0.74 per 100,000 population as contrasted with 0.41 per 100,000 population in the southern states. According to Faure,[29] the greatest incidence of thrombosis is from December to February. He believes that grippal infections are responsible for this increase. Probably the seasonal and the geographic variations are due to the vasospastic effect of cold and its effect on the blood flow. Another factor which predisposes to intravenous clotting, probably because of its vasospastic effect, is smoking. As a prophylactic measure we believe it is desirable for patients who are to have an extensive operative procedure to refrain from smoking for a number of days before the contemplated operation and for approximately ten days postoperatively.[86] Intravenous clotting frequently occurs in certain families, so that a constitutional diathesis to this condition cannot be denied. As emphasized by many observers, the type of individual who is likely to develop an intravenous clot is fat, pale skinned, asthenic, and weak muscled. The tendency is an inherited one and recognition of the con-

stitutional disposition is of importance from a prophylactic standpoint, in order that measures can be instituted to prevent thrombosis. Obesity also is a predisposing factor. Henderson[39] found that the average weight of patients with thrombo-embolism was thirteen pounds greater than normal. Barker and his co-workers[6] state that 4 per cent of patients who weighed less than 200 pounds developed thrombo-embolism, whereas 8 per cent of those weighing more than 200 pounds developed the same complication. In 3,680 patients on whom intestinal operations were done, thrombo-embolism occurred in 3.2 per cent of those who weighed less than 200 pounds and in 7.1 per cent of those who weighed more than 200 pounds. Of 156 postoperative fatalities studied by Snell,[114] the cause of death was thrombo-embolism in 30.7 per cent. Debility and anemia are predisposing factors in intravenous thrombosis. In the former, probably the increased coagulability of the blood, and the decreased cardiac tone in the latter predisposing to circulatory retardation are responsible for the intravenous clot. Anemia predisposes to intravenous clotting because of two possible causes. First, as emphasized by Drinker, Drinker, and Kreutzmann,[26] following hemorrhage there is a relative increase in the cellular elements of the blood which increases its coagulability, and, second, anemia may predispose to thrombosis because of its secondary effect on the cardiovascular system resulting in diminution of cardiac tone which favors circulatory retardation. Likewise, polycythemia is a predisposing factor in intravenous clotting because the increased number of erythrocytes increases the viscosity of the blood which favors coagulation.

The absorption of noxious substances from traumatized cells following invasion by malignant disease increases the clotting tendency of the blood. In fact, the increased clotting tendency in malignancy is so great that it has been suggested that the increased coagulability of the blood might be used as a diagnostic test for cancer. Trousseau[121] directed attention to the causal relationship of cancer and thrombosis and stated that frequently the first manifestation of an internal cancer is peripheral phlebitis. Sproul[115] and more recently Kenney[53] have emphasized the high incidence of venous thrombosis as a complication of carcinoma of the body or tail of the pancreas. Sproul[115] found that in 56 per cent of cases of carcinoma of the body or tail of the pancreas a single thrombus was present, whereas in 31.3 per cent the venous thromboses were widely disseminated. In 33⅓ per cent of Kenney's cases[53] of carcinoma of the body or tail of the pancreas there were multiple venous thromboses. Carcinoma of the head of the pancreas showed no increased incidence of venous thrombosis. It is interesting also that in Kenney's series the tumor was, in each instance, of the mucinous type. It is his belief[53] that these tumors secrete an abnormal substance or an excessive amount of a normal substance which is concerned with blood clotting. Sproul suggested that the increased incidence of intravenous thrombosis associated with carcinoma of the tail or body of the pancreas was due to in-

creased coagulability resulting from increased digestion of fats because of increased pancreatic secretions which in turn results in increased absorption of vitamin K from the intestine. That this hypothesis is not correct, however, is suggested by the investigations of Morton, Shearburn, and Burger,[78] who showed that the administration of an excess of vitamin K does not cause excessive thrombosis and intravenous clotting.

Of great importance in determining the site at which intravenous clotting is likely to occur, particularly in phlebothrombosis, is circulatory retardation. It is probably the principal reason why clotting usually occurs in the lower extremities because in these areas the greatest amount of vascular stasis occurs. As is well known, the movement of venous blood is dependent upon a number of factors, the chief of which are the vis a tergo through the capillaries, the negative pressure within the thorax, and the contraction of the skeletal muscles. As a result of an operative procedure, any illness, or cardiovascular disease the vis a tergo is definitely diminished. In the first instance this is due partly to decreased cardiac function, but also is due to vasoconstriction as DeBakey and I[82, 86] have emphasized repeatedly. In the other two instances it is due mostly to the decrease in cardiac function. The negative pressure within the thorax is definitely less marked following a laparotomy or in severe illness than is found normally, because hypopnea is the rule. Deep breathing is likely to be painful following laparotomy particularly that involving the upper part of the abdomen, and for this reason the patient usually breathes in a shallow manner, thus favoring circulatory retardation in the venous system of the lower extremities. The relative immobility of the lower extremities while in bed is of great importance in favoring vascular stasis. Whereas the patient who has been operated upon or who is otherwise ill moves his upper extremities, he is very likely to keep his lower extremities immobile predisposing to circulatory retardation in the lower extremities. Also, patients who have had a laparotomy because of decrease in intestinal activity and associated dilatation of the gut (ileus) may have increased intra-abdominal tension. This tends to compress the abdominal veins, produce venous stasis in the lower extremities, and favor clotting. According to Neumann,[80] there are a number of anatomic structures which produce localized vascular stasis and predispose to thrombosis in the particular area, that is, the plantar veins, the veins of the calf, and the veins of the thigh. Posture may favor vascular stasis. The use of Fowler's position, particularly with the flexion of the leg on the thigh at the knee, causes stasis below the popliteal vein because of the dependency of the leg and also because of the kinking of the popliteal vein. According to Friedländer,[33] with the patient in the prone position vascular stasis of the lower extremity is favored because of the uphill course of the femoral vein to join the iliac at the pelvic entrance.

As previously mentioned, injury to tissue as result of an operation, an accidental trauma, a delivery, or invasion by infection or malignant disease results in increased coagulability of the blood because of absorption into the blood stream of noxious substances derived from the traumatized cells. The increased blood coagulability is the result of changes in the plasma and the formed elements of the blood. The changes in the plasma consist of increased viscosity, hypoproteinemia, hyperglobulinemia, increased fibrinogen content, increased antitryptic power, increased peptidase, increased calcium content, and decreased carbon dioxide combining power. Because of the increase in globulin and decrease in albumin there is a disturbance in the albumin-globulin ratio which is evidenced by an increased erythrocytic sedimentation rate.[10, 17, 24, 28, 41, 54, 71, 72, 116, 117, 119, 126] The peptidase content of the plasma is an indication of the cell destruction according to vonSeemen[111] and the aseptic destruction of the cells produces a decreased blood stability and a decrease in antithrombin with an increased tendency toward clotting. Associated with this is a disturbance in the ratio of calcium and potassium ions and also a disturbance in the albumin-globulin ratio in that the globulin is increased and the albumin decreased. Lambret and Driessens[64] showed that postoperatively there is a rise in polypeptides which reaches a maximum at about the fifth day and the more prolonged, the more traumatic, and the more histolytic the operative procedure, the greater is this increase. In addition to the changes in the fluid element of the blood which predispose to clotting there are alterations in the cellular elements of the blood. Thrombocytes and leucocytes become increased, and erythrocytes become decreased. Of great importance also is the increased agglutinability of the formed elements of the blood, particularly the thrombocytes. This is probably due to a change in the electrical charge of the formed elements which results in the loss of the normal repulsion of these elements with a resultant attraction to one another. This increased agglutination tendency causes clumping and is probably responsible for the initiation of a thrombus. The change in the electrical charge of the formed elements is the result of the disturbance in the albumin-globulin ratio referred to previously.[10, 17, 24, 28, 41, 54, 71, 72, 111, 116, 117, 119, 126] Hausser[38] found that the increased agglutinability of the platelets paralleled the increased tendency toward thrombosis. He found that the increased agglutination tendency of the platelets is particularly marked after hernia repair and after abdominal operations, and was greatest in older persons.

Whereas the changes in the blood and blood constituents resulting from tissue injury and associated circulatory retardation are responsible for the intravenous clotting in phlebothrombosis, in those cases in which there is an inflammatory process of the vein wall (thrombophlebitis) the clotting is due principally to injury of the endothelium by the inflammatory process. In the latter instance the inflammation of the vein

wall is usually the result of bacterial invasion, as in puerperal thrombophlebitis and in many cases of postoperative thrombophlebitis associated with febrile reaction. As emphasized by Koster[60] and Kaufmann,[52] the microorganisms generally gain entrance to the venous system through the medium of the perivenous lymphatics. Relatively rarely the vein intima may be involved by bacteria present in the blood stream which process has been designated by Rokitansky[104] as secondary phlebitis in contradistinction to the primary form in which the venous involvement begins in the wall and extends to the lumen. The latter occurs relatively infrequently and is seen only in those cases in which there is an actual pyemia.

Pathology.—Whereas previously it was thought that most intravenous clotting occurred principally in the larger veins, such as the iliac and femoral, more recent pathologic studies have demonstrated that the clotting begins primarily in the more peripheral veins. Roessle[103] found in complete autopsies of 324 consecutive cases that thrombosis occurred in the deep veins of the calf in 88 persons over 20 years of age. Of this number 38 had thrombosis of the femoral vein, in 10 of whom death was due to pulmonary embolism. Neumann[80] in a similar study of 165 unselected patients dying from a variety of causes found thrombosis in 100. The foot veins were involved in 71 per cent, the leg veins in 87 per cent, and the thigh veins in 22 per cent. Solitary thrombi occurred in the calf veins more frequently than in the other veins. Solitary calf vein thrombosis occurred in 39 per cent, solitary plantar vein thrombosis in 12 per cent, and both calf vein and leg vein thrombosis in 57 per cent. In many of these the thromboses had apparently begun in the calf veins. There were no cases in which femoral thromboses occurred without involvement of the calf veins. Similar observations have been made by Bauer,[9] Hunter and his collaborators,[48] and Frykholm.[36] Frykholm[36] in a dissection of 133 venous thromboses observed that 85 per cent were found distal to the profunda in the femoral vein and most of these were below the knee. The involvement of the left side is more frequent probably because the greatest amount of vascular stasis is on this side for definite anatomic reasons.

Thrombophlebitis may occur in normal veins or in diseased veins. The previously normal veins in which thrombophlebitis is likely to occur are: (1) the cavernous cerebral sinus following infection of the upper lip or nose; (2) lateral cerebral sinus following infections of the middle ear and mastoid process; (3) ileocolic superior mesenteric and portal veins following acute suppurative processes in the intestinal tract, especially of the appendix; (4) ovarian, hypogastric, and common iliac veins following suppurative processes in the puerperal uterus; and (5) superficial and deep veins of the lower extremities following infections of the pelvis and the lower extremity.[92] Thrombophlebitis of the cavernous sinus fortunately occurs relatively infrequently, but is almost invariably the result of maltreatment of localized suppurative lesions

about the upper lip and nose. The absence of subcutaneous fat in the upper lip, the active muscular supply of the lip, movement of which exerts a pumping action on the venous radicles of the labial plexus, and the inability of the veins in this region to collapse are responsible for the involvement of the cavernous sinus through the facial, angular, and ophthalmic veins in cases of phlegmon of the upper lip. Thrombophlebitis of the portal veins following suppurative processes in the cecum and rectum occurs more frequently than is commonly appreciated. According to Gage, Garside and myself,[93] thrombophlebitis of a portal vein occurs in from 0.1 to 1 per cent of all cases of acute appendicitis and in about 5 per cent of patients dying of appendical peritonitis. Involvement of the ovarian and hypogastric veins following uterine infections occurs not infrequently in puerperal infections and is likely to follow septic abortion. Miller[76] found in 100 reported cases of puerperal pyemia in which a vein ligation had been done and in which localization was stated, involvement occurred in the following veins: one ovarian vein, 75 times; two ovarian veins, 5 times; one hypogastric and one ovarian, 6 times; one common iliac, 8 times. The diseased veins in which thrombophlebitis is likely to occur are varicosities of the veins of the lower extremities and of the hemorrhoidal veins.

In addition to these cases of thrombophlebitis there are many other cases of thrombophlebitis which are differentiated from those mentioned by the fact that the lesions are not suppurative lesions. Thrombophlebitis involving the cavernous sinus, the lateral sinus, and the portal veins and the ovarian and hypogastric veins are usually associated with suppuration and the clinical picture is characterized by recurrent chills and the septic type of temperature. On the other hand, most cases of thrombophlebitis are caused by a nonsuppurative inflammatory process involving the deep venous system of the lower extremity. This is typified by the phlegmasia alba dolens which is so well known to clinicians. Since there is no suppuration in these cases there is no liquefaction of the clot and a septic clinical picture is not seen.

The vascular changes in thrombophlebitis can be divided into those occurring in the perivenous tissue and those in the vein wall itself. The perivenous changes consist principally of a lymphangitis. According to Koester,[59] the thrombophlebitic process is in reality a lymphangitis of the veins in which the infection is carried to the veins by means of the lymph channels. The importance of perivenous lymphangitis has been emphasized by Karsner,[51] Homans,[43] and Homans and Zollinger.[45] As a result of the perivenous involvement, fibrinous exudation into the perivascular spaces and the accumulation of perivascular fluids resulting in edema are likely to occur. Kaneko[50] was able to produce intravenous thrombi experimentally by the perivenous implantation of streptococci, staphylococci, and colon bacilli. In addition to the perivenous changes there are changes within the wall of the vein, consisting primarily of hyperemia, cellular and serous exudation, and a destruction of the

endothelium, which is probably responsible for the thrombosis. The intravascular changes which occur in thrombophlebitis consist of the development of thrombi. The clot or thrombus produced in thrombophlebitis differs from that produced in phlebothrombosis in that the former is attached to the vein wall. As Aschoff[3] described, there are two types of thrombi, the white and the red, the white usually being associated with thrombophlebitis in which there is a maximum change in the wall of the vessel resulting in a deposition and agglutination of the platelets on the vessel wall. There also becomes adhered to the vessel wall in this area, leucocytes and fibrin, resulting in a white thrombus. On the other hand, in those cases of intravascular clotting in which there are few or no changes in the vascular endothelium, but in which thrombosis occurs because of stasis in the vessel together with other factors which favor coagulation, the thrombus is similar in many, if not all, respects to an extravascular clot. This is designated as a red thrombus or coagulation thrombus. It has much the same relative proportions of blood elements as are found in the circulating blood. It is not firmly attached to the vein wall as is the white thrombus, because the former is not the result of endothelial destruction. The white thrombus, because of the destruction of vascular endothelium, is firmly attached to the vein wall and has little tendency to become detached. On the other hand, the red thrombus is attached only loosely to the vein wall and it is this type of thrombotic process that is particularly likely to give rise to pulmonary embolism. In those cases of thrombophlebitis, however, in which there is suppuration resulting in liquefaction of the coagulum, portions of the thrombus may become detached resulting in septic emboli.

The clinical picture in intravenous clotting is dependent upon the lesion in the vein, and in nonsuppurative thrombophlebitis, because of the inflammatory reaction and because of the associated vasospasm resulting from impulses originating in the thrombophlebitic segment, there is diminished vascularity to the extremity producing pain, swelling, and a persistence of fever. In the cases of suppurative thrombophlebitis in which because of the liquefaction of the clot by the suppurative process portions of infected thrombi become detached, repeated chills and aseptic temperature results. In the patient with a phlebothrombosis, in whom there is no inflammatory reaction early, there are few or no clinical manifestations but because the thrombus is only loosely attached to the vein wall, detachment can occur resulting in one or more nonfatal or massive fatal pulmonary emboli. In thrombophlebitis, because of the inflammatory process in the vein wall, there is usually a pyrexia which varies in degree with the severity of the infection and the localization of the thrombophlebitic process. Everything else being equal, the more severe the infection, the more marked is the febrile reaction; and also the larger the vein involved, the greater is the systemic reaction. In addition to fever, these patients have pain in the

region of the involved vein, and swelling of the involved extremity. The classical example of deep thrombophlebitis is phlegmasia alba dolens, in which cases the pyrexia ranges from 101° to 103° F., associated with severe pain and swelling in the involved extremity. The fever in thrombophlebitis is probably due to the inflammatory reaction of the vein wall. Previously, the pain in thrombophlebitis was thought to be due to the inflammation and irritation of the vein wall, but DeBakey and I[86] have demonstrated quite conclusively that the pain is due to ischemia, as evidenced by the prompt relief of the pain following the re-establishment of the normal blood supply to the extremity by blocking the sympathetic impulses. The edema which previously was thought to be due to increased venous pressure caused by the obstructing thrombus in the main venous channel is due also to ischemia. That obstruction of the main venous channel is not the cause is evidenced by the fact that ligation of the same vein done aseptically seldom produces edema and that in the patients treated by sympathetic anesthetization the edema associated with thrombophlebitis disappears while the clot is still present. We have shown both clinically[83-85] and experimentally[22] that the edema is secondary to severe arteriolar spasm in the homolateral extremity resulting from the vasoconstrictor impulses originating in the thrombophlebitic segment which are carried over the sympathetic nervous system. This vasoconstriction is responsible for the whiteness of the skin as designated by the term phlegmasia alba dolens. Because of the extreme vasoconstriction of the arterioles and ischemia resulting in relative anoxia of the capillary endothelium, an increased permeability of the capillary endothelium results. This permits excessive exudation of the intravascular fluid out of the vascular system into the perivascular spaces and accounts for the rapid production of edema. Once the fluid gets out of the vascular system, there is difficulty in its getting back for two reasons: first, because wound absorption is interfered with because of the increased venule pressure resulting from venule spasm, and, second, because the pump which is responsible for the movement of lymph, namely arteriolar pulsation, is lost. Although the patient with thrombophlebitis has marked symptoms there is little or no danger of embolism, because of the fixation of the clot to the vein wall, except in the case in which a propagating coagulation thrombus occurs proximal to the area of thrombophlebitis, or in the case of suppurative thrombophlebitis in which liquefaction of the clot occurs.

The patient with phlebothrombosis may have no symptoms. He usually has no pain, has little or no fever, and there is usually no swelling of the extremity. We have observed that frequently the patient has a sense of impending disaster. According to Bahls,[4] the patient is likely to be restless. There is almost invariably tenderness over the involved vein and the calf and plantar veins are frequently the original sites. Tenderness in the calf or on the plantar aspect of the foot is of importance. Pain in the calf or popliteal area resulting from dorsiflexion

of the foot with the leg extended is of diagnostic importance as suggested by Homans.[42a] Not infrequently there is an increasing pulse rate out of proportion to temperature elevation, which finding has been emphasized by Mahler[73] and DeBakey and me.[86] Mahler described this as stepladder pulse. In a suspected case the determination of the erythrocytic sedimentation rate is of importance, and is probably the result of the alteration of the albumin-globulin ratio.[10, 17, 24, 28, 41, 54, 71, 72, 116, 117, 119, 126]

Diagnosis.—The diagnosis of thrombophlebitis is not difficult. In fact usually the patient calls the attention of the physician to the lesion because of the pain, tenderness, and swelling. In addition to this, elevation of temperature usually signifies some lesion. There is tenderness along the course of the involved vein and in the skin of the extremity. If the involved vein is a superficial one, there is also redness in this area. On the other hand, if the deep veins are involved, the extremity is cold and whiter than normal due to the associated spasm of the arterioles. There is usually a pitting edema. Phlebothrombosis can be diagnosed definitely only by demonstrating the presence of the venous obstruction by means of visualization of the venous system (phlebography).[86] Although we originally thought that phlebography should be done in all cases of suspected phlebothrombosis, we now feel that in a suspected case of phlebothrombosis the diagnosis can be accepted and appropriate therapy instituted immediately. In any patient who has had a pulmonary embolism immediate steps must be taken to prevent further emboli because following one embolism there is the likelihood of another. Zink[131] has shown that in 70 per cent of patients with fatal pulmonary embolism there was a previous nonfatal pulmonary infarct, the result of embolism. We had an opportunity to see a patient who had had five nonfatal pulmonary infarctions before curative therapy was instituted.

Treatment.—There are probably few conditions in which prophylaxis can be so readily accomplished and yet is so important as in intravenous clotting. The importance of this has been repeatedly emphasized by DeBakey and me.[82-88, 92] Because cardiovascular disturbances with the resultant circulatory retardation are of such great importance in the development of intravascular clotting, it is imperative in any patient who has tissue injury resulting from operative, accidental, or puerperal trauma or from invasion by infection or neoplastic disease, that normal cardiovascular function be maintained or early re-established. This is particularly true in older persons in whom cardiovascular disease is more liable to occur. The value of prophylaxis is exemplified by vonJaschke's[49] results. Whereas in a series of 2,053 operations the incidences of thrombosis and fatal embolism were 1.75 and 0.6 per cent, respectively, in a comparable series of 1,362 operations in which the patients were systematically digitalized preoperatively, the corresponding incidences of thrombosis and fatal embolism were 0.9 and 0.5 per cent. Koenig[58] found that following the use of sympatol (a cardiac

stimulant) in 2,000 cases postoperatively, the incidences of thrombosis and embolism decreased from 6.2 to 0.95 per cent. Similarly, Frauendorfer[31] observed a decrease in the incidences of thrombosis and embolism from 10.6 to 2.3 per cent and in the mortality rate from 2.3 to 0 per cent.

Circulatory stasis is favored by the vasoconstrictor action of tobacco, and for this reason it is desirable for patients who are to undergo an operative procedure to refrain from smoking for a period of a few days before any contemplated operation, and in the immediate postoperative period.[86] In this way we believe that circulatory stasis can be minimized and the precipitating effect of vasoconstriction prevented.

Of great importance from a prophylactic standpoint, we believe, is the routine use of compression bandages applied to the lower extremities from the toes to the groin.[86] It is routine in our clinic to use this measure in all patients 45 pears of age and older who undergo an operative procedure. This is of value not only in patients with varicosities in whom stagnation is more likely to occur, but also in patients whose superficial veins are normal. By the application of compression bandages stagnation of the blood in the superficial veins is obviated and the blood flow in the deep venous system is increased, thus preventing circulatory retardation. The value of compression of superficial veins in intravenous clotting was first stressed by Fischer.[30] Leun,[69] over a nine-year period, used compression bandages prophylactically in patients in whom he feared thrombosis, such as individuals with varicosities, circulatory disturbance, or other predisposing factors. In 280 cases, 500 elastic compression bandages were applied. In three cases the treatment was a failure in that thrombosis occurred. In two of these slight thrombosis occurred because the bandage was not applied tightly enough, and the third patient died of pulmonary embolism, but the autopsy showed that the thrombus originated from a pelvic vein and not from a leg vein. In obese patients in whom an elective operative procedure is done, it is imperative that there is a reduction in weight before the contemplated operation, because obesity is an important predisposing factor to intravenous clotting.[82, 86] Also, it is desirable that foci of infection be eliminated since they too predispose to intravenous clotting.

Another important prophylactic preoperative measure is hydration and remineralization. As many patients who are subject to operation are suffering from nausea, vomiting, or diarrhea, there is likely to be a loss of fluids and electrolytes. It is not known whether the correction of these disturbances is beneficial because of the correction of increased viscosity and dehydration or because of the detoxifying effect of the electrolytes. Prima[99] is of the opinion that administration of sodium chloride solution has a definite detoxifying action which tends to prevent intravascular clotting. Anemia and other blood dyscrasias should be corrected as prophylactic measures, since these conditions predispose

to intravascular clotting. Lockhart-Mummery[79] and Donald[25] directed attention to the greater likelihood of thrombosis in anemia. Donald[25] reported three cases of profound anemia in which the patients developed fatal pulmonary embolisms, and believed that the thromboses were to a large extent caused by the anemia. Drinker, Drinker, and Kreutzmann[26] demonstrated that following hemorrhage there is an increase in the cellular elements which probably increases the coagulability of the blood.

In addition to preoperative prophylactic measures, a great deal can be accomplished in the prevention of intravenous clotting during the operative procedure. Since injury to tissue is an important factor in changing the blood constituents, increasing the tendency toward thrombosis, it is imperative that trauma be reduced to a minimum. Sharp dissection and careful hemostasis, avoiding mass ligation, are of great importance. Lambret and Driessens[64] found that following an operation there was a rise in the polypeptides, which reaches its maximum on about the fifth day and that this was more prolonged, the more traumatic and the more histolytic the operative procedure. Since absorbable suture material (catgut) produces maximum tissue reaction, it is desirable that nonabsorbable suture material be used, unless there is some definite contraindication. Meade and I[75] believe from both clinical and experimental investigations that cotton is the best suture material available at the present time, because it gives the minimum amount of reaction and the best healing. The incidence of infection is lower with cotton which in itself tends to decrease tissue destruction.

The prevention or correction of dehydration and circulatory collapse during the operative procedure, both of which favor circulatory retardation, is imperative. The circulatory collapse may be the result of blood loss, chilling, or operative trauma. In many cases it is necessary to administer saline, blood, or plasma. Chilling should be prevented because by virtue of its vasoconstrictor effect it predisposes to circulatory retardation. Chilling is also detrimental in another way in that it increases the viscosity of the blood as shown by Barbour and Hamilton,[5] who demonstrated that exposure to cold causes a loss of fluid from the vascular channels into the tissues.

Postoperatively, prophylaxis also should be practiced. Dehydration and loss of electrolytes must be corrected because, due to the loss of fluid and electrolytes from the gastrointestinal tract, an increased viscosity of the blood is likely to occur as has been demonstrated by Zarubin[128] and Bolognesi,[13] Posture is frequently of great importance in predisposing to circulatory retardation. The placing of the patient in Fowler's position with flexion of the thigh on the abdomen and flexion of the legs on the thighs at the knees results in compression of the popliteal vessels and should be avoided. If the head-up position is desirable the patient should never be placed in a sitting position but should be kept flat on the bed. The frequently employed pillow beneath the

knees when the patient is in the supine position should not be used because it favors slowing of the blood in the legs. It is the rule in our clinic that when the patient is first returned to his room he is placed in the head-down (Trendelenburg) position in order to favor the return of the venous blood from the lower extremities to the heart. This procedure has been recommended by many others.[8, 11, 21, 27, 33, 44, 49, 79, 107] The head-down position is maintained until the patient can actively move his extremities which by virtue of the muscular contractions forces the venous blood toward the heart. The value of the Trendelenburg position in preventing postoperative thrombosis is illustrated by Schmid's[105, 106] experience. Prior to 1935, before the use of the position was routine, the incidence of postoperative thrombosis was 3.1 per cent whereas after elevation of the foot of the bed was instituted in all cases the incidence dropped to 0.5 per cent. The respective incidences of fatal pulmonary emboli were 0.9 and 0.3 per cent.[105] As soon as the patient can actively contract the muscles of the lower extremity, this is insisted upon. We have him contract the calf muscles against a resistance by either placing a foot piece at the foot of the bed against which the foot can be ventroflexed or have an attendant hold the patient's toes while he flexes his feet against the resistance. Wangensteen[124] advocated having the patient move his extremities "a thousand times a day." Reis,[101] Richardson,[102] Boldt,[12] and others[40, 56, 61, 97, 123, 127] were early advocates of the movement of the legs while the patient is still in bed. Gamble[37] and deTakats and Jesser[23] have suggested the use of a bed bicycle, whereas Adams and Boehme[1] believe that the foot exercises are much preferable to the use of a bed bicycle. Kirschner[55] uses elaborate gymnastic procedures, accompanied by music and under the direction of a gymnast. The importance of mobilization is emphasized by Potts,[98] who observed that whereas thrombosis and embolism are common in patients who are confined to bed with fractures in plastic encasements, they are rare in ambulatory patients with arm, leg, shoulder, or spine fractures in similar encasements.

At the present time, there are a number of advocates of early ambulation which we have used for a number of years, although we are not as radical as many in getting our patients out of bed on the day of the operation or the first postoperative day. Unquestionably, this decreases the incidence of intravenous clotting. Campeanu[19] reported 1,300 cases, many of which were severe, in which the patients were allowed to walk directly from the operating room to the ward and to take gymnastic exercises immediately afterward, including even jumping. Zava,[130] who gets his gynecologic patients up either on the first or second day, states that in more than 6,000 cases there has not been a single embolism. The value of early ambulation is emphasized by vonJaschke,[49] who found among 300 patients who were allowed up relatively late, there were 2 per cent with thromboses and 1 per cent with fatal emboli, whereas in

387 cases in which early ambulation was used the incidence of thromboses was 0.5 per cent and there were no fatal emboli. In the Essinger University Clinic from 1906 to 1912 there were 1,504 operative cases in which the patient got out of bed at the end of the second week with the incidences of thrombosis and fatal embolism of 2.63 and 1.4 per cent, respectively. In the same clinic, from 1912 to 1918, there were 2,053 operations following which the patients got out of bed between the second and fifth days with the corresponding incidences of 1.75 and 0.6 per cent. The need of getting patients out of bed relatively early is exemplified by the investigations of Smith and Allen[113] in which it was shown that postoperatively, beginning on the fifth day, the circulation time was increased, and that on the tenth day it was approximately 50 per cent greater than the preoperative average. Eighty-two per cent of the individual patients showed increases of four or more seconds at some time after operation.

Another measure which favors the movement of venous blood is the increased negative thoracic pressure resulting from deep breathing. The importance of this should be emphasized to the postoperative patient because usually by the descent of the diaphragm the intra-abdominal tension is increased causing pressure on the abdominal wound and pain. Because of this the patient is likely to breathe in a shallow manner. We insist upon our patients taking twelve to fifteen deep breaths every hour during their waking hours and we much prefer this being done voluntarily. If, on the other hand, they are unable or will not cooperate, it is desirable to secure deep breathing by means of carbon dioxide inhalations.[37, 55, 57, 82, 86] The prevention of increased intra-abdominal tension by the avoidance of tight compression bandages on the abdominal wall and the prevention of ileus is of importance in decreasing stasis of blood in the lower extremities. Increased abdominal tension also may be due to the decreased action of the diaphragm and the splinting of the abdominal wall as emphasized by Patey[95, 96] and Frimann-Dahl.[35]

Since vasoconstriction occurs in all cases following operation it is desirable to overcome the peripheral vasospasm by vasodilatation. This can be done by either the application of heat to the extremities or reflexly producing vasodilatation by applying heat to some other part of the body. For many years we have applied heat to the abdomen in patients who have had laparotomies because we are convinced that it exerts a beneficial effect on the gut tone. In this way we have secured reflexly vasodilatation in the extremities and have minimized circulatory retardation. Leriche,[68] Kvale,[63] and DeBakey and I have shown that postoperatively a peripheral vasoconstriction occurs. Smith and Allen[113] also showed that postoperatively there is a definite slowing of the peripheral circulation and that this is more marked when the extremity is cold.

Anticoagulants, such as hirudin, heparin, or dicumarol, might be used prophylactically. Whereas the use of these substances probably

is not justified routinely in all patients who are operated upon, their use should be seriously considered in patients in whom there is a thrombosing tendency as determined by history of previous intravenous clotting or a history of a clotting tendency in the family. The value of anticoagulants used prophylactically is shown by Barker's[7] results at the Mayo Clinic. Dicumarol was administered postoperatively to thirty patients, who had either thrombosis or embolism previously. None developed thrombosis or embolism although the estimated incidences without an anticoagulant in these cases were 40 per cent thrombosis or embolism and 10 per cent risk of fatal embolism. In a group of 259 patients who had had abdominal hysterectomy in which the estimated incidences of thrombo-embolism and fatal pulmonary embolism were 4 and 0.7 per cent, respectively, there were no thromboses or emboli following the prophylactic use of dicumarol. DeBakey and I[92] believe that the principal use of anticoagulants is as a prophylactic measure and not in the treatment of thrombosis once it has occurred, because in such instances they are of little or no value in the treatment of a preexisting thrombus and are of value only in preventing the propagation of the thrombus. At the same time, their use is likely to give the physician a false sense of security that everything is being done for the patient and he may neglect to use those therapeutic measures which are essential. On the other hand, the use of anticoagulants is not without danger and must be carefully controlled.

Although we believe that most, if not all, cases of intravenous clotting can be prevented by the institution of appropriate prophylactic measures, patients will be seen in which actual thrombosis has occurred, and in which active therapy is necessary. Once clotting has occurred it is important to differentiate between thrombophlebitis and phlebothrombosis. In nonsuppurative thrombophlebitis, because the symptoms are the result of arteriolar spasm, the treatment consists of overcoming the vasoconstriction by anesthetization of the regional sympathetic ganglia. This is essential because as long as arteriolar spasm and resulting ischemia persist there is a persistence of the clinical manifestations which may last for months or even years. The pain and swelling are the result of ischemia. The persistence of fever also is probably due to the ischemia resulting in an interference with the normal resolution of the inflammatory process. I believe that the most efficacious way of producing vasodilatation is the interruption of the sympathetic impulses by anesthetization of the regional sympathetic ganglion with procaine. DeBakey, Burch and I[22] have been able to demonstrate graphically both clinically and experimentally that in thrombophlebitis a marked spasm of the arterioles and venules of the homolateral extremity occurs. There is also some spasm of the contralateral arterioles, although this is much less marked than on the affected side. Following the procaine block of the homolateral sympathetic ganglia the arteriolar pulsations return to normal and the clinical picture graphically changes.

The relief of pain is immediate, occurring as soon as the anesthesia is complete. In approximately 90 per cent of instances, the pain does not recur. In the remaining cases, however, a second injection is required to relieve the patient permanently of pain. Fever and edema disappear rapidly. The temperature returns to normal within forty-eight hours in about 65 per cent of cases. In about 5 per cent of cases the pyrexia lasts longer than eight days. The swelling of the extremity, instead of lasting for months and even years, subsides very quickly with the re-establishment of the normal blood supply, because of the normal re-establishment of the arteriolar pulsations which are responsible for the movement of lymph. In our cases, edema completely disappeared within four days in over one-half of the cases, and in only 5 per cent of cases did it last longer than twelve days. These patients can be discharged from the hospital early because of the rapid subsidence of their clinical manifestations. Sixty-two per cent of our patients were discharged from the hospital within four to eight days after institution of therapy, and only 10 per cent remained in the hospital more than twelve days.

The technique of lumbar sympathetic block has been described in detail in previous publications,[83, 84, 90] but is, in brief, as follows: The patient is placed in the lateral recumbent position. This position is used rather than the prone position which is usually employed for the lumbar sympathetic block in peripheral arterial disease, because usually a patient with thrombophlebitis is too ill to be placed in the prone position. The thighs are flexed on the trunk in an attempt to straighten the lumbar curve. The sites of puncture in the skin are determined by taking points approximately two fingerbreadths lateral to, and on a horizontal level with, the spinous processes of the first, second, third, and fourth lumbar vertebrae on the affected side. The spinous processes are chosen because the transverse processes are on a level with them. A cutaneous wheal is made at each one of these points. Special (B.D.) 20 gauge short beveled needles, 14 cm. in length, are introduced at each point vertical with the skin surface until the transverse process is reached. The transverse process is used as a landmark, because, whereas there may be considerable difference in the thickness of the subcutaneous fat and the sacrospinal muscle in an obese, muscular man and a thin, emaciated woman, there is relatively little difference in the thickness of the bodies of their vertebra. After striking the transverse process, the direction of the needle is slightly changed, either above or below the transverse process, and the needle is inserted approximately two fingerbreadths beyond the process. The point of the needle then lies on the anterolateral surface of the body of the vertebra where the sympathetic chain lies. Through each needle, 5 to 10 c.c. of 1 per cent procaine are injected after first aspirating to determine that the point of the needle is not within the vessel. The procaine anesthetization is repeated daily as long as the patient has fever, because it is

our belief that the persistence of fever is an indication of the persistence of the inflammatory process and that as long as the inflammatory process exists in the vein there is a likelihood of vasospastic impulses being set up. Although the pharmacologic effect of procaine should last one to one and one-half hours, the physiologic effect of the anesthetization of the sympathetics lasts a good deal longer, at least twenty-four hours. Generally, two to three daily blocks are sufficient to bring about complete restitution of the process. In addition to procaine blocks of the regional sympathetic ganglia, patients with thrombophlebitis should have their extremities wrapped from the toes to groin and mobilization instituted. This is particularly important in order to prevent a propagating red thrombus proximal to the thrombophlebitic segment. If this is done there is no danger of embolism occurring in the uncomplicated case of thrombophlebitis.

Although the treatment of uncomplicated thrombophlebitis is that of conservatism as outlined, suppurative thrombophlebitis must be treated radically because of the detachment of infected emboli resulting from liquefaction of the clot. In the patient who has had a pelvic infection with the development of a septic clinical picture consisting of recurrent chills and septic febrile reaction, ligation of the venous system above the site of the involvement is imperative, because if this is not done the sepsis and fatal pulmonary embolism are likely to occur. A typical example of this is puerperal sepsis especially following criminal abortion in which the thrombophlebitic process involves the venous channels draining the uterus. In such cases rapid progression of the process with breaking off of the infected emboli is likely to result in a blood stream infection and fatality. Hunter,[47] in 1793, was apparently the first to apply measures to combat this possibility, by compressing the vein above the suppurative lesion. Lee,[67] in 1865, ligated a vein above the thrombophlebitic process in two patients suffering from this condition. In 1880, Zaufal[129] successfully ligated the internal jugular vein in the treatment of pyemia originating in the internal ear. Viereck,[122] in 1900, showed statistically the value of vein ligation in such cases. In a collected series of 108 cases, 89 patients recovered. Freund,[34] in 1898, was one of the first surgeons to apply the method in gynecology. He performed ligation and excision of the thrombosed ovarian vein and broad ligament in two cases. These procedures were unsuccessful. Several years later Bumm[14-16] and Trendelenburg[120] performed venous ligation in puerperal pyemia, the former advocating ligation by the transperitoneal route and the latter by the extraperitoneal route. Miller,[77] in 1917, collected 197 cases of puerperal pyemia treated by venous ligation. Fifteen were approached extraperitoneally and 182 transperitoneally. The gross mortality was 51.6 per cent. In 1921, Martens[74] reported eleven gynecologic cases of thrombophlebitis in which ligation of the ovarian vein as well as that of the internal or common iliac was done. In two cases the vena cava was successfully ligated.

Recovery followed in seven of the eleven cases. Collins,[20] Weinstein[125] and other members of our gynecologic service have ligated the vena cava in twenty cases of severe puerperal pyemia with recovery in all but one case. We have ligated the inferior vena cava in three cases with extensive suppurative thrombophlebitis of the pelvic veins resulting from infections in the lower extremity.

Whereas there has been considerable controversy concerning the optimum time for the ligation of the vein in suppurative thrombophlebitis, it is our belief that it must be done early, and that the high mortality rates reported by earlier observers are the result of operating upon moribund patients. Trendelenburg[120] suggested that these patients be operated upon immediately after the first chill. On the other hand, there are many who believe that one should wait until the disease has become chronic before operation. It is suggested that ligation not be done until the patient had vaccinated herself against the infection. We now believe that by procrastination the patient becomes vaccinated not against her infection but against life, because most of them die. The patient who is obviously ill, and who has recurrent chills, should be operated upon early. Otherwise a fatality is likely to occur. Whereas the operative procedure is associated with little or no risk, the advantages to be derived from it are immeasurable. As early as 1912, Huggins[46] advised exploratory laparotomy in every suspicious case when the diagnosis is in doubt, because, in his opinion, "the danger from thrombophlebitis is far more threatening than the risk of operation," if done early. If an infarction has already occurred, operation should be performed immediately and procrastination in such cases is likely to mean disaster. The absence of chills in no way precludes the possibility of a septic thrombophlebitis. Schollenberg[108] states that, on the basis of the material at the Zurich University Women's Clinic, in the cases in which the second chill was taken as an indication for operation, 67.4 per cent of the patients were operated upon unnecessarily and in cases in which the third chill was taken as an indication for operation, 56.2 per cent were operated upon unnecessarily. The technique of the operative procedure may vary according to the individual operator. A distinct advantage of the transperitoneal route is that it is possible to visualize and ligate all four of the veins draining the uterus or even the vena cava itself, if it is found necessary, through a single incision. This operation is associated with a greater risk, however, because of the greater shock associated with the transperitoneal approach and also because of the potential danger that infection of the peritoneum will occur from division of the infected vessel. Not only should the vessel be ligated but it should be divided, and preferably a segment should be removed. Simple ligation of the inferior vena cava is all that is necessary in those cases in which it is possible to get well above the point of involvement. We have employed proximal venous ligation of the femoral vein in five cases of suppurative thrombophlebitis of the deep

veins of the lower extremity, of the brachial vein in two cases of similar involvement of the deep veins of the upper extremity, of the ovarian vein in one case of puerperal sepsis, and of the inferior vena cava in three cases of pelvic suppurative thrombophlebitis following infection of the lower extremity, all with immediate cessation of chills and prompt recovery of the patient.[92]

The treatment of phlebothrombosis in contradistinction to thrombophlebitis is always radical. As mentioned previously, this type of intravenous clotting is accompanied with few or no manifestations. These patients do not appear ill but they represent potential fatalities, because the clot not being attached to the vein wall is likely to become detached and result in a fatal pulmonary embolism. Unless measures are taken to prevent the clot from getting into the systemic circulation after it becomes detached, a tragedy will result. In suspected cases of phlebothrombosis and also in those cases in which a pulmonary infarct has occurred, ligation of the involved vein above the thrombus is imperative. Because in many instances thrombosis is bilateral, it is desirable to do a bilateral femoral ligation. Sears[109, 110] states that all patients with thrombosis of the calf veins should have a proximal vein ligation as soon as the diagnosis is made. Thrombectomy has been advocated by Läwen[66] and Kulenkampf,[62] the former extracting a thrombus through an opening in the femoral vein, the latter through the saphenous opening. Both attempt to save the deep venous system by suture of the vein wall. Lange[65] also advocates thrombectomy, but Freund[34] states that ligation should also be done. Allen and his coworkers[2] report an increasing incidence of femoral vein ligation at the Massachusetts General Hospital. In 1937, one femoral vein was tied; in 1938, none; in 1939, eight; in 1940, five; in 1941, fifty-five; and in 1942, 211. The right side was ligated in 46 per cent of the instances, and the left in 54 per cent. Sixty-one per cent of the operations were unilateral, and 39 per cent were bilateral. Whereas theoretically thrombectomy and suture of the vein seem desirable, and although the experimental work of Hintze and Zollenkopf[42] appears to support the contention that these veins again function, we believe that not only is it unnecessary to attempt to save the vein, but that it is actually dangerous. Shackelford and Whitehill[112] report a case of multiple pulmonary emboli in which a cure was obtained by ligation of the left common iliac vein at its junction with the inferior vena cava. Although we originally contended that it was desirable to expose the vein above the site of involvement and ligate rather than attempt to aspirate the proximal portion of the clot, we now believe that the latter procedure is preferable. Exposure of the femoral vein in the upper part of the thigh can be performed with considerably less operative trauma than exposure of the external and common iliac veins through a retroperitoneal approach. The operation can be done under local analgesia, and can be done in the patient's bed, but is preferably done in the operat-

ing room. The patient is placed on the operating table with the trunk on a higher level than the thigh to increase the venous pressure in the femoral vessels. The femoral vein and its branches at its upper extremity are exposed. Care is taken not to manipulate the vein any more than is absolutely necessary, because a thrombus which is frequently difficult to detect before the vein is opened can be easily dislodged. Ligatures are carefully and loosely placed around the common femoral above the saphenous, around the profunda femoris, and around the superficial femoral. The long saphenous is doubly clamped close to the femoral and divided between the clamps. The distal end is ligated and the edges of the proximal end caught either with mosquito forceps or fine sutures. Into the proximal end a glass suction tube is introduced passing proximally into the femoral and external iliac veins, and gentle aspiration is maintained, in order that a contained thrombus can be aspirated. Aspiration is maintained until a free flow of blood occurs from the proximal portion, indicating an absence of clot between the opening in the saphenous vein and the inferior vena cava. Because of the elevation of the trunk and upper part of the body there will be an increase in the venous pressure and expulsion of the clot is favored. The femoral is then ligated above and below the saphenous opening. If there is free bleeding from the profunda femoris it need not be ligated, but if it also contains a thrombus it is to be ligated as well as the common femoral.

By the interruption of the involved vein above the site of the embolism in phlebothrombosis, one can prevent embolism from occurring, and in this way prevent infarction and fatality.

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DISASTER FOLLOWING FEMORAL VEIN LIGATION FOR THROMBOPHLEBITIS; RELIEF BY FASCIOTOMY; CLINICAL CASE OF RENAL IMPAIRMENT FOLLOWING CRUSH INJURY

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DESPITE the contributions of Ochsner, Fine, Allen, Waugh, and others, there is as yet no unanimity of opinion among surgeons as to the most adequate type of therapy to employ in postoperative thrombophlebitis. The results published by Fine and Frank indicate that most such cases, in which the presence of the disease has been demonstrated by venograms, are relieved, both of local evidences of the disease and of the danger of embolism, by high ligation of the veins above the involved area. Allen and his associates found no deleterious effects to follow such high ligation, as ligation of the femoral vein above the fossa ovalis, and recommended free use of such ligation in cases of postoperative thrombophlebitis.

In the past few months one patient so treated at the University of Minnesota Hospitals has developed serious complications following high ligation of the femoral vein, which should be brought to general attention.

CASE REPORT

D. M. (Hospital No. 739518), a 59-year-old janitor, came to the University of Minnesota outpatient department, Dec. 18, 1943, complaining of a tender mass in the left groin. The mass had developed in the previous three months, during which time he had been wearing a truss for a right inguinal hernia. Questioning showed that at the age of 16 he had had rheumatism, during which his elbows had been swollen and painful. He had had a left inguinal hernioplasty in 1930, pleurisy about 1935, backache "all his life," and had been an excessive user of alcohol.

Physical examination showed a small indirect inguinal hernia on the right side, kept well reduced by a truss. There was a scar from the old hernioplasty on the left side. Just below this scar was an egg-shaped mass 7 by 3 cm., hard, fixed, and tender. The left testis was atrophic.

The man was sent to the outpatient tumor clinic because the marked induration and fixation of the mass suggested a neoplastic process rather than a hernia. He was admitted to the hospital, December 21, for excision biopsy of the mass. Exploration, December 24, under combined spinal and cyclopropane anesthesia revealed a femoral hernia containing incarcerated, necrotic omentum. The inguinal ligament was divided by the surgeon to facilitate removal of the sac, and a modified McVay-Harkins type of repair was made, using No. 3 Champion silk suture. Sulfathiazole was implanted in the course of the repair.

In the first three days postoperatively the patient had a temperature as high as 101° F., but following the fourth day remained afebrile until January 6, thirteen days after surgery. January 1, however, eight days after surgery, he presented a positive Homans' sign on the left side, and tenderness and local heat in the left

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calf. One per cent procaine sympathetic block of the left first and second lumbar levels at once, and of the first, second, and third levels the next day, relieved the patient entirely.

January 5, twelve days after surgery, swelling and tenderness appeared around the wound, and sulfathiazole therapy was begun, 1 Gm. every six hours, by mouth. January 7, a small amount of purulent exudate was evacuated from the wound, and the temperature commenced to rise, reaching 105.4° F. on January 9, sixteen days after surgery, when the sulfonamide was discontinued because of the feeling that this represented drug fever. (See Fig. 1.) The temperature dropped almost to normal in the ensuing three days. The wound had apparently healed by January 12. Nausea and vomiting, January 10 and 11, were attributed to the sulfonamide.

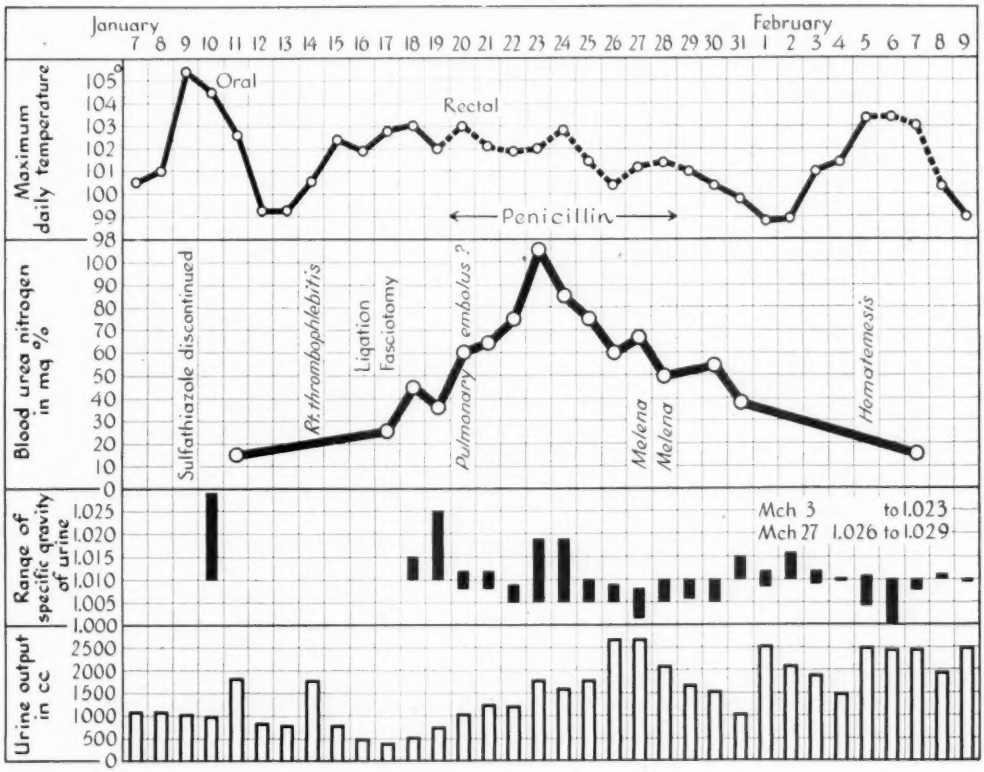
January
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
February
1 2 3 4 5 6 7 8 9
Maximum daily temperature
105° 104 103 102 101 100 99 98
Oral
Rectal
Penicillin
Blood urea nitrogen in mg %
100 90 80 70 60 50 40 30 20 10 0
Sulfathiazole discontinued
Rt. thrombophlebitis
Ligation
Fasciotomy
Pulmonary embolus ?
Melena
Melena
Hematemesis
Range of specific gravity of urine
1.025 1.020 1.015 1.010 1.005 1.000
Mch 3 to 1.023
Mch 27 1.026 to 1.029
Urine output in cc
2500 2000 1500 1000 500 0

Fig. 1.—Variations in blood urea nitrogen level, urinary output, and urinary specific gravity ranges in the period following relief of engorgement of the right leg by fasciotomy.

The patient was to have been dismissed January 14, twenty-one days after the hernioplasty, but on the morning of this day he developed swelling, tenderness, and a positive Homans' sign in the *right* lower leg. Lumbar sympathetic block failed to give relief, either January 14 or when repeated January 15.

January 16 the patient looked sicker than at any time earlier (see Fig. 1). The circumference of the right calf (measured 15 cm. below the lower margin of the patella) was 38.5 cm. as compared with 37 cm. a day earlier and 30 cm. a week earlier. At noon the right leg was pinker and definitely warmer than the left, and there were numerous engorged veins, particularly below the knee. A firm thrombus could be palpated extending from the knee upward to a point 12 to 15 cm. below the inguinal ligament in or overlying Hunter's canal.

Three courses of therapy were considered: (1) more procaine injections, which seemed inadvisable because of earlier experience with fatal embolus in cases with little inflammatory reaction; (2) anticoagulant therapy, not adopted because the process seemed too rapid for dicumarol and because labor trouble at the hospital had made help too inadequate to embark on the use of heparin; (3) the ligation of the femoral vein above the saphenous opening.

At 3:00 P.M., January 16, removal of the junction of the right femoral and saphenous veins was completed under 1 per cent procaine block anesthesia. The segment removed contained both liquid blood and thrombus. At the end of this resection a small spurting vessel was found between the artery and the vein distally. It spurted a colorless clear liquid, not blood, and it was also ligated.

Upon removal of the drapes, the whole leg was seen to be engorged and deeply cyanotic, and the patient complained of pain in the leg and of numbness of the sole of the foot. The calf now measured 39.8 cm. in circumference, and the tightness of the skin soon became marked enough to render the surface shiny. The pulse on the dorsum of the left foot could be easily felt, but the right dorsalis pedis pulse was very feeble, though definitely present.

Procained lumbar sympathetic block was employed at once, without more than minimal improvement, and the temperature of the right leg began gradually to fall.

About 7:00 P.M., January 16, the blood pressure dropped sharply to 40/0. Administration of 1100 c.c. of plasma and 500 c.c. of whole blood returned the pressure to normal levels. This amount was repeated the following day. At 9:00 P.M., January 16, the measurements of the two legs were as indicated in Table I.

TABLE I

CIRCUMFERENCES OF LEGS SIX HOURS AFTER RIGHT FEMORAL VEIN LIGATION

	RIGHT	LEFT
Thigh (15 cm. above top of patella)	60 cm.	44 cm.
Knee	33 cm.	36 cm.
Calf (15 cm. below bottom of patella)	40 cm.	30 cm.
Ankle	24 cm.	20 cm.
Roughly calculated volume	9½ liters	6¼ liters

The loss of fluid into the right leg was calculated to be at least 3 liters. The patient was observed in steep Trendelenburg position overnight.

Skin temperatures were observed by the use of a thermocouple. At 9:00 P.M. there was no consistent difference in the two legs, but by the following noon the temperatures in the right leg were definitely dropping. Tissue tensions were also determined late in the evening of January 16.

TABLE II

SUBCUTANEOUS TISSUE TENSION DETERMINATIONS EIGHT HOURS AFTER RIGHT FEMORAL VEIN LIGATION

	RIGHT (CM. OF WATER)	LEFT (CM. OF WATER)
Thigh	24	4.5
Knee	37	16.5
Calf	19.5	20
Ankle	43	1

The temperature of the right leg continued to fall, the tension of the skin increased slowly, and the leg became more blue and black in color. Reanastomosis of the vein did not seem feasible, and division of the deep fascia was therefore performed at 6:00 P.M., January 17, after a good spinal anesthesia had failed to bring improvement. Fasciotomy was suggested by Dr. O. H. Wangensteen in line with

the experimental findings of Jepson. Longitudinal incisions were made extending from about 5 cm. below the knee joint to about 10 cm. above the ankle medially and laterally and from 5 cm. above the knee joint to a point 10 cm. below the groin medially, and to a corresponding level on the lateral side of the leg. The wound of the femoral ligation was re-explored at this time. There had been no hemorrhage there, and the wound was found clean and dry. The femoral artery could be felt pulsating normally in the depth of this wound, but in the course of the medial fasciotomy a finger was placed beneath the sartorius muscle, and no pulsation could be felt at this level. The muscles were very edematous, and bulged hugely from the fasciotomy incisions at all points. In the lateral thigh incision there was arterial bleeding; this was found nowhere else. Sulfanilamide powder (10 Gm.) was packed into the wounds with petrolatum packing. Following fasciotomy, and while the patient was still on the table, the leg rapidly became warmer below the knee.

January 20, three days after fasciotomy, the patient complained of chest pain on the left side, and physical signs suggested consolidation. Because of persistent fever and a shaking chill, penicillin was started (10,000 Oxford units every three hours by intramuscular injection). It was administered thus until January 28. On January 24, a roentgen film of the chest indicated an infarction of the left middle lobe. The temperature gradually dropped under penicillin therapy.

January 28, abdominal cramps, distention, vomiting, and melena appeared, confirming the fear that mesenteric venous occlusion might complicate the picture. For the next week vomiting persisted, often bloody in character, and the patient remained critically ill. Thereafter, improvement in the gastrointestinal functions gradually took place.

By March 1, the patient presented clean, granulating fasciotomy wounds except for some necrosis in the lower medial incision. Motor power in this extremity had been lost completely below the knee, and sensation was present, but impaired. Ability to flex and extend the knee was partial.

On March 2, the patient developed pain in the *left* calf, with a positive Homans' sign, and tenderness in the calf and along the course of Hunter's canal. There were petechiae overlying Hunter's canal, and there was swelling of the entire extremity. The leg was cold except for a small area of local heat overlying the femoral vein. Following three days of roentgen therapy, the pain seemed to diminish slightly, but the swelling became more marked, and consequently heparinization was undertaken, using the continuous intravenous infusion method in such fashion as to maintain a capillary tube-method clotting time of about twenty-five minutes. Dicumarol* was started simultaneously in sufficient dosage to keep the prothrombin time ten seconds above the control level. Heparin was discontinued, March 11, because the prothrombin time had been adequately prolonged, but dicumarol was given until the end of the month.

Under this therapy, all evidences of thrombophlebitis disappeared in one week, and have not recurred.

The patient was kept in the hospital until early July for physiotherapy and because of a polyarthritis which now has disappeared. At the time of dismissal there was a small unhealed area at the lower end of the lower medial fasciotomy incision only, and all evidences of thrombophlebitis had been absent for three months. Function has not yet returned to the muscles of the right lower leg, but the patient is able to stand and to bear some weight (Fig. 2).†

*Supplied to Dr. C. J. Watson through courtesy of Abbott Laboratories. The author is indebted to Dr. Watson for permission to use the drug in this case.

†This patient returned to the hospital in December, 1944, with what appeared to be recurrent thrombophlebitis of the right leg. He has had one attack of thrombophlebitis since July, 1944, in the left leg also. Therapy with dicumarol has been effective each time.

Recent detailed questioning has shown that the patient had a mild attack of thrombophlebitis in 1942.

It is thought that interference with venous return developed in this patient by the phlebitic involvement of those collateral veins about the upper end of the femur which ordinarily serve as a pathway for return blood flow after high femoral and saphenous vein ligation. Salvage of the leg by fasciotomy a day later must have been possible because of the opening of additional collateral channels.

Of particular interest in this patient is the evidence of renal damage apparent in Fig. 1. Following fasciotomy, the patient developed uremia despite a good urinary output, and there appeared to be a simultaneous loss in the ability of the kidneys to concentrate the urine. The damage suggests that which has been described by Blalock as following prolonged use of the tourniquet experimentally. It was temporary in this instance, as the blood urea nitrogen level fell, and the ability of the kidneys to concentrate returned in about six weeks.

Fig. 2.—Photograph of patient six months after femoral ligation. The legs have returned to normal size, and the patient can bear some weight on the right foot.

COMMENT AND CONCLUSION

The possibilities of exploration of the collateral venous return in the upper thigh by venograms in the presence of thrombophlebitis are being explored. There is some tendency in this clinic in the meantime toward

conservatism in femoral ligation in those cases in which more than one venous bed has been involved. Femoral vein ligation, use of anticoagulants, strict conservatism, sympathetic procaine block, and roentgen therapy are all being used in an effort to evaluate the indications for each, but this evaluation has not as yet been accomplished.

This case is presented as a warning that indiscriminate use of femoral vein ligation above the fossa ovalis for symptoms of thrombophlebitis is not devoid of danger.*

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*In the recent past another instance of inadequate collateral venous return has been encountered. The patient is a 19-year-old girl who has had a total colectomy for chronic ulcerative colitis and who has had repeated attacks of superficial and deep thrombophlebitis bilaterally. Thrombophlebitis returned one year after right saphenous ligation for superficial disease, and right lumbar sympathectomy early in 1944 relieved the symptoms of the disease in that leg until December, 1944, when right deep thrombophlebitis again developed. A venogram showed a single narrow vein draining the extremity. Under pentothal anesthesia a loose catgut strand was placed under the femoral vein. Venous pressure at the ankle was 7 cm. of blood without compression of the femoral vein, but with occlusion by means of the strand the venous pressure at the ankle rose to 38 cm. of blood in less than two minutes. The entire skin of the extremity assumed a dusky, blotchy appearance during compression of the vein. Ligation was not done.

It is suggested that venous pressure measurements be made at the ankle during compression of the femoral vein under direct vision prior to ligation in those patients in whom there have been repeated or widespread thrombophlebitic episodes.

THE SENSATION OF GAS STOPPAGE DURING THE ONSET OF ACUTE APPENDICITIS

With Illustrative Cases

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IN PRACTICE the surgeon delays his diagnosis of acute appendicitis until pain localizes. The appendix may perforate while the surgeon waits.

Precise study has revealed that the onset of acute appendicitis may be made the foundation of accurate diagnosis even prior to localization because of a symptom complex, the gas stoppage sensation.[1] It is the purpose of this paper to illustrate the gas stoppage sensation as a basis for diagnosis.

THE ACCEPTED VIEW OF ONSET

By onset is meant those first hours of vague abdominal discomfort prior to localization. So vague may be this discomfort as to cause some patients to forget or to disregard anything before the pain in the right iliac fossa. Therefore "it is well in taking the history of any acute abdominal condition to focus the patient's mind on the beginning of the attack," as Richardson[2] wrote in 1930.

Homans[3] in 1940 described the onset of acute appendicitis in a manner little short of pathognomonic. He wrote as follows:

> A very typical attack in a young adult is ushered in by pain, which appears to be due, at an early stage at least, to overdistension of the appendix. Thus it partakes of the nature of a colic—a sustained colic, not an intermittent one, such as is caused by a violent spasm of the appendix itself. Moreover, like many other acute pains arising within the peritoneal cavity, it can seldom be exactly located but is referred to the center of the abdomen, the region of the umbilicus, or the epigastrium. It varies from an almost unbearable ache to a feeling of nagging discomfort, but is usually severe and associated with nausea, perhaps vomiting. Very rarely is it relieved temporarily by the passage of gas or a movement of the bowels. After several or many hours it subsides, to be exchanged for a feeling of soreness in the right iliac fossa, that is, in the region of the appendix itself.

THE GAS STOPPAGE SENSATION

Note the essential elements of Homans' description: a sustained colic, vaguely located in the midline (and associated with nausea and vomit-

The author's father, E. L. Keyes, M.D., of New York, helped in preparing this paper.

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ing), rarely relieved temporarily by the passage of gas or a movement of the bowels.

If the phrase about nausea and vomiting in parenthesis is omitted, an almost perfect description of the sensation of gas stoppage remains, though the emphasis is not where it should be. The sensation of gas stoppage merits the name because it is always a desire to pass gas downward rather than up and is characteristically relieved little, if at all, by whatever gas or feces does pass. It is a subjective sensation—a symptom, not a sign. Fitz[4] long ago recorded a characteristic of gas stoppage when he noted that "a cathartic or laxative may be demanded by the patient."

Homans is influenced by the formula made traditional by Murphy[5] to write that the "discomfort . . . is associated with nausea, perhaps vomiting." What Murphy actually stressed is the order of symptoms, and not their association. He made this clear by writing "the order is all-important in making a diagnosis: First pain . . . . referred at first usually to the epigastrium . . . . gradually changing to the right iliac fossa or to the location of the inflamed appendix. Second, nausea and vomiting."

Nausea and vomiting, however, do not always occur. (See Table I.) The true characteristic of the onset, prior to localization, is the sensation of gas stoppage, persisting whether or not the bowels move or gas is passed by rectum.

Gas stoppage is usually present at onset regardless of whether subsequent localization is "typical," "atypical," or absent entirely.

It is also essential to note that the gas stoppage sensation characterizes the onset of acute appendicitis and only the onset. When an acute attack begins with the "pain of localization" there is no sensation of gas stoppage. Such cases are relatively uncommon.

TABLE I

THE GAS STOPPAGE SENSATION IN TEN PATIENTS WITH APPENDICITIS

CASE	THE ONSET					LOCALIZATION	PATHOLOGY
	COULD PATIENT PASS BY RECTUM		NAUSEA?	VOMITING?	DURATION OF ONSET (IN HR.)		
	GAS?	FECES?					
1	No	Yes	Yes	Yes	19	Typical (?)	Acute
2	No	Yes	Yes	No	17	Typical	Acute
3	Yes	Yes	No	No	7	Typical	Ruptured
4	No	No	No	Yes	12	Atypical	Ruptured
5	No	No	No	No	1½	Typical	Subacute
6	No	No	No	No	48	None	Ruptured
7	No	No	Yes	No	28	None	Ruptured
8	Yes	Yes	No	Yes	24	None	Acute
9	No	No	Yes	No	30	Atypical (?)	Subacute
10	No	No			24	Typical	Subacute

If the patient does not mention spontaneously the sensation, and few patients do, there are two, sometimes three, questions, necessary to elicit the information.

1. "At onset, did you feel as if gas or something were stopped up inside?"

To this question the patient with gas stoppage usually answers Yes.

2. "At onset, did you feel that passing gas by rectum or moving the bowels would relieve the feeling?"

To this the patient answers Yes.

3. (For patients able to pass gas or to defecate during onset.) "Was the feeling completely relieved by passing gas by rectum or by a movement of the bowels?"

To this the patient answers No.

EXAMPLES OF THE GAS STOPPAGE SENSATION IN PATIENTS

CASE 1.—A 22-year-old medical student, not yet studying surgery, reported because of abdominal discomfort. The onset was gradual, about 2 P.M. the day before, March 19, 1944. Discomfort was dull and generalized in the lower abdomen, and to the patient it felt as though gas was stopped up inside him. He felt if he could pass gas by rectum he might obtain some relief, but he could pass no gas. The discomfort increased and moved upward about the umbillicus. Lying quiet helped it; eating increased it. The bowels moved without any gas passage about 9 P.M., but the movement gave no relief. There was nausea and about midnight the patient vomited three or four times. He felt better about 9 A.M. when the pain localized somewhat in the right iliac fossa, and at which time he was first seen. He took no laxative. The temperature was 98.4° F., the pulse 78. He looked somewhat sick. When first examined there was slight tenderness one inch to the right and below McBurney's point, and slight tenderness by rectum. All physical signs disappeared completely after he lay in bed about one hour and other observers then seeing him found him asymptomatic and without abdominal or rectal signs. The leucocytes were 10,850 at 10 A.M., with 1 per cent eosinophiles, 10 per cent stabs, 75 per cent segments, 8 per cent lymphocytes, and 6 per cent monocytes.

The diagnosis by two of us familiar with gas stoppage sensation was subacute appendicitis; the diagnosis by two others was uncertain. At operation a swollen, red appendix was removed. It was constricted at the base with distal swelling, clinically acute. The histologic diagnosis was acute appendicitis.

This patient had had a previous attack which he said was similar and for which he consulted a fellow staff member on July 7, 1943. Following is his note: "Vague onset yesterday afternoon with pain in lower right quadrant. Nausea and vomiting this morning, no diarrhea. Pain, however, has not been acute today. He states he feels better now. The belly is flat and not particularly tender. Deep pressure over the cecum elicits only slight tenderness. Leucocytes 14,600, stabs 3 per cent, segments 88 per cent, lymphocytes 8 per cent. Impression: Enteritis, although mild retrocecal appendicitis cannot be excluded. Recommend bed rest and liquid diet."

Comments on Case 1.—An intelligent patient told a clear story spontaneously. He answered the three questions, Yes, Yes, No. Localization was indefinite. Operation revealed acute appendicitis.

CASE 2.—A 24-year-old medical student reported complaining of pain in the belly which began June 1, 1944, at about 9 A.M. Following are the patient's words copied

verbatim as he talked with me at 3 P.M., June 2, before I operated on him, names and irrelevant questions being omitted.

"Yesterday morning at 8 o'clock I had a normal bowel movement following breakfast. At 9 o'clock I first noticed mild cramps in the upper epigastrium. They didn't interfere enough with classes so I kept on with my work until 11:30 A.M. Cramps were still mild at that time. Then I ate chili and drank a glass of milk, and went to Clinical Pathological Conference. I remained there five or ten minutes; the cramps became much worse. Quite a few fellows smoke in there; I felt nauseated and went home. At about 2 P.M. I had a bowel movement, the same as the one I had had this morning. I thought the bowel movement would clear everything up, but it didn't seem to make any difference, so I went back to bed and slept till 6 P.M. I didn't feel like eating any supper so I came to see Dr. ——— who said I had nonspecific enteritis. He gave me some papaverine tablets. They didn't help. About 8 or 9 P.M. I felt some distention. I felt that if I could pass a lot of flatus or belch, it would help, but I couldn't. I tried to pass flatus or to have a bowel movement but I couldn't. I slept from 11 P.M. to 2 A.M., then I felt tenderness in the right lower quadrant on palpation so I saw another doctor, who said I had nonspecific enteritis and gave me nembutal. I slept from 4 A.M. to 8 A.M. and on waking felt pain in the right lower quadrant. I took a glass of milk and poached egg on toast, then slept from 9 A.M. until noon. I noticed that the cramps were not relieved and everything was about the same, with the same amount of tenderness in the right lower quadrant. In the last half hour there has been more tenderness in the right lower quadrant."

I asked him the following questions referring to the gas stoppage sensation.

"At onset, did you feel as if gas or something was stopped up inside?"

"No, not then; but I did feel that way around eight or nine o'clock last night." (Eleven or twelve hours after onset.)

"At onset, did you feel as if you might have obtained relief by defecating or by passing gas per rectum?"

"No, not then, but around eight or nine o'clock last night I felt if I could pass flatus it would help and I made three unsuccessful attempts at stool."

Examination showed a temperature of 99.8° F.; pulse 90; leucocytes 16,300, with eosinophiles 2 per cent, stabs 8 per cent, segments 68 per cent, lymphocytes 15 per cent, and monocytes 5 per cent. The patient looked sick; the face was flushed, the pupils wide. He lay on his back with the thighs flexed. He looked dehydrated, although the tongue was moist, not furred, and the breath sweet. The abdomen was distended, with hyperesthesia in the right lower quadrant and tenderness and spasm all over the right lower quadrant, most marked about one inch below McBurney's point. Rebound tenderness. No retraction of the right testicle. Tenderness on right side by rectal examination. Diagnosis: acute appendicitis.

Fluids were given intravenously preparatory to operation but, during the few hours between admission and arrival in the operating room, the temperature suddenly rose to over 104° F. (anesthetist's report) and the pulse to 132. The patient looked poorly; consequently he was sent back to his room and plasma and sulfadiazine were administered, with opiates, etc., postponing operation over twelve hours. Operation, finally performed by me about forty-two hours after onset, revealed a gangrenous appendix ruptured in two places by a large ovoid, soft olive-colored fecalith one centimeter in diameter. About the appendix was a local accumulation of pus and there was marked increase of dirty fluid in the peritoneum, suggesting generalized peritonitis. Appendectomy. Histologically acute appendicitis.

Comments on Case 2.—The gas stoppage was established by 2 P.M., marked by evening, yet the diagnosis was missed twice and the appendix

was ruptured when removed. A dangerous illness might have been spared the patient by early diagnosis.

CASE 3.—A 25-year-old medical student complained of abdominal pain, which had begun suddenly the night before, as a sharp epigastric pain. In a few minutes it had become severe and griping and ten minutes later spread over the upper abdomen, as far down as the umbilicus. He thought of something to bring the gas up but this feeling, he said, was not nausea. A few minutes later he passed a lot of gas and a large soft stool. This relieved him somewhat and then the discomfort was dull and diffuse, a soreness all over the abdomen. He felt shaky and broke into a cold sweat. He took hot tea with some temporary relief. An hour after onset he passed a large fluid stool, although no laxative had been taken. The movement helped somewhat, but he passed no gas. He slept restlessly.

I questioned him as follows: "Try to describe the feeling at onset."

"I can't describe it."

"At onset, did you feel as though gas or something was stopped up inside?"

"Yes."

"At onset, did it feel to you as if passing gas by rectum or moving the bowels would relieve the feeling?"

"Yes."

Localization of pain began about 6 A.M., in the right iliac fossa. He ate no breakfast. He lay flat on his back for relief.

There had been many previous attacks, notably one six months before, of two hours' duration. At that time he had an urge to defecate and made two efforts; the first resulted in a bowel movement, the second did not. But he could not answer the three questions as to these former attacks.

He looked somewhat sick. The tongue was slightly furred. A point of maximum tenderness was found halfway between the right anterior superior spine and the umbilicus with referred pain, no rebound tenderness, and no tenderness by rectum. Temperature was 98.6° F.; pulse 88; urine, 1 plus albumin; leucocytes 13,200, with eosinophiles 1 per cent, stabs 16 per cent, polymorphonuclears 78 per cent.

Diagnosis: acute appendicitis. An acutely inflamed appendix was removed. Histologically acute appendicitis.

Comments on Case 3.—This was the most enlightening history of the lot. A medical student called his initial symptom pain, griping, dull soreness, then "I can't describe it." This real discrepancy in the story of an unusually intelligent young man shows how vague the discomfort was to him and the three questions crystallized his notions.

And to confuse the issue still further, to one of the surgeons, asking the three questions without reference to any particular time, the patient, thinking he referred to the present, answered, "No" to all of them for, localization having taken place, the gas sensation had disappeared.

When the questions were repeated with strict reference to onset he gave the answers, Yes, Yes, No.

CASE 4.—A 51-year-old hospital stretcher-bearer complained of cramps in the stomach and vomiting. Vague onset at about 2:30 P.M. caused him to take an enema, but he then disregarded the pain. Suddenly that evening at 6:30 P.M., prior to admission, cramps became severe. In his own words, there were "cramps in my stomach right after I'd eaten supper and took a ride downtown. I felt them coming on and the jar of the bus would affect me so that I wanted to get off. I felt

if I could get my bowels to move it would go away. I got off the bus, went into a tavern, and sat on the toilet about fifteen minutes. The bowels did not move and I couldn't pass any gas or anything. (At this time he vomited once.) Then I came out and I was still having cramps. All this time the cramps were in the lower part, way down over my bladder. I went to a drugstore and got some red drops. I took a few drops in water and it seemed to relieve me some. Then I went out in the park and sat down on a bench and the cramps came back again. Then I came home and went to bed and took some more red drops. I kept going to the toilet, thinking my bowels would move. Finally I took two laxative tablets about 10:30 P.M. About midnight the bowels semed to work gradually. Their action would relieve for a bit, just for a few minutes, but I was never really comfortable and I never slept more than five minutes all night. I was up and down all the time (and vomited seven or eight times). Toward morning the pain went down to my scrotum and I was in for it. So I went to the doctor.''

He answered the three questions, Yes, Yes, No.

The patient appeared very sick and was holding his lower abdomen. Temperature was 98.6° F., pulse 108, leucocytes 18,500. The abdomen was obese and there was marked tenderness in both lower quadrants, particularly the right, with rigidity. There was tenderness by rectum.

Only the resident staff saw this patient before operation and to them the diagnosis was not clear. It was agreed that the patient had peritonitis, probably due to appendicitis. Acute intestinal obstruction was ruled out. Some staff members unfamiliar with the gas stoppage sensation thought the original lesion a ruptured gastric ulcer or sigmoid diverticulum.

Operation revealed a ruptured appendix and generalized peritonitis. Histologically acute appendicitis.

Comments on Case 4.—Note the gradual onset suddenly becoming severe; also note how bowel consciousness dominated the clinical picture until the patient took a laxative and how the vomiting thus induced was what actually brought him to the hospital.

CASE 5.—A clinical clerk's history of a 27-year-old fellow student reads, ''Chief Complaint: dull aching pain in right lower quadrant of fourteen hours' duration. Present illness: Last night about nine the patient had a feeling of epigastric distress and discomfort with a desire to pass flatus but inability to do so. This was followed in about one and one-half hours by a dull aching pain in the right lower quadrant, localized in the region of McBurney's point. This continued throughout the night. The following morning the patient had no appetite and passed two loose bowel movements. Today he has felt generally well except for constant dull aching pain. No nausea or vomiting. However, patient has not felt like eating today, although he took a cup of coffee and a slice of toast for breakfast, a coke and a cookie for lunch, and nothing since that time. At present complains of mild aching pain and tenderness in the right lower quadrant.''

Examination showed a somewhat sick patient. The temperature was 97.6° F.; pulse 92; leucocytes 8,900, with stabs 2 per cent, segments 60 per cent, lymphocytes 34 per cent, monocytes 8 per cent. The abdomen was flat. There was local tenderness and rebound tenderness lateral to McBurney's point and tenderness by rectal examination. Diagnosis: acute appendicitis. Operation revealed an appendix swollen at its midportion. Appendectomy. Histological diagnosis: subacute appendicitis.

Comments on Case 5.—A straightforward case of acute appendicitis by every standard. It is interesting only because of the physicians

who examined the patient did not elicit the usual answers because, as happened in Case 3, he did not succeed in making clear to the patient that the questions referred to the onset. So much do the two pains differ that even a "mild" localized pain turns the patient's thoughts away from consideration of the onset discomfort.

CASE 6.—A 44-year-old hospital carpenter was referred by another physician in 1940. He complained of abdominal discomfort and was actually suffering from a sensation of gas stoppage. At that time no one could have had an inkling of this.

The history then taken was of lower abdominal cramps beginning two days previously and followed by no nausea or vomiting. He had taken milk of magnesia with slight result. Examination revealed no fever; leucocytes, 6,200; no localization of pain, and only a questionable tenderness at McBurney's point. Though he did not look very sick, he was sent to the hospital where he had a complete examination by the medical, surgical, urological, and otolaryngological services. He had a gastrointestinal series and a barium enema. No diagnosis had been arrived at when suddenly, twelve days after onset, the temperature and the leucocyte count rose; the patient clearly had a pelvis peritonitis, and the abdomen was explored. A perforated gangrenous appendix was removed.

Four years later the patient was questioned, in the light of our new beliefs. When asked what brought him to the hospital, he answered, "Not exactly a pain but a gnawing right in the center of my stomach." He said this "began on Monday, July 8, 1940. It started in the night. I felt O.K. the night before. It came on slowly. When I woke up in the morning, it seemed just a dull stomachache that I thought was cramps. I came to work thinking it would wear off. I didn't see a doctor till 1 P.M. Wednesday. In the meantime I got some milk of magnesia and took that with no relief. It bothered me all Monday night and still bothered me when I got up Tuesday and was a little worse. Tuesday I attended a funeral. The cramps seemed to be growing a little worse all the time so I went home from the funeral and stayed home the rest of the day. I felt pretty bad the next morning. I came in the hospital to see a doctor."

He then answered questions as follows:

"Do you remember trying at onset to move your bowels?"
"Yes, I tried to do that."
"With what results?"
"No results then."
"No gas?"
"No, there wasn't."
"Did the gnawing sensation at onset feel as if gas was stopped up inside you?"
"That's just the way it felt. I couldn't pass it one way or the other."
"Which seemed to be the way it wanted to pass?"
"It seemed to be more through the rectum."

Comment on Case 6.—The diagnosis was missed because pain did not localize. Four years after the event the story was elicited that would have saved him a dangerous illness. One wonders how he managed to remember those vague onset discomforts so accurately.

CASE 7.—I was the patient, taken sick on vacation. When I was admitted to the hospital, the admission note under date of April 20, 1941, was as follows: "Chief complaint: abdominal pain.

"Present illness: On Wednesday, four days ago, this 41-year-old white male physician was chilled while exercising. The next day he had general malaise and

a temperature of 101° F. He was out of town at the time but returned immediately and was seen at home by Dr. ——— who thought his condition was due to sinusitis. Except for headache, the patient had no subjective symptom of upper respiratory infection, but soon after returning to St. Louis his sinuses began to drain more than usual. His general malaise continued. He had three normal bowel movements and yesterday in the morning he began to experience abdominal pain. This was characterized as 'tugging' in character and generalized in situation. About 1 P.M. yesterday, after a light lunch, the pain became quite severe but let up toward evening, although it never disappeared completely. A few hours after a light supper the pain became very severe. Still of a 'tugging' nature 'as though someone were pulling on my mesentery.' He was kept awake all night and finally called Dr. ——— at 3 A.M. today. At this time there was generalized tenderness on examination with slight localization in the right lower quadrant. This morning the patient had no stool and passed no gas per rectum. Leucocytes 15,000. He took no catharsis but last night had a low enema with passage of a little gas and considerable relief. He had no nausea and no vomiting but took little fluid or food by mouth because it aggravated the pain. He was not febrile during the period of abdominal pain. He had no urinary frequency, burning, dysuria, pyuria, or hematuria.

"Temperature, 99.4° F.; pulse, 80; respirations, 20.

"Appears moderately acutely ill with sallow muddy complexion. Breath fetid, pharynx granular and injected. The abdomen is moderately obese, with little distention. There was no spasm or muscle guard. Minimal tenderness in right lower quadrant, medial and below McBurney's point. Gurgling sensation felt in the area of the cecum. Costovertebral area clear, genitals normal. There was no rectal tenderness or masses.

"Impression: sinusitis, probably subsiding appendicitis."

That evening, the symptoms having subsided, leucocytes having fallen to 8,200, and the temperature being normal, it was voted that I might return home. But I protested that, having lost a brother by acute appendicitis, I should prefer mine out.

April 23, appendectomy. The appendix was found gangrenous and ruptured. Histologically acute appendicitis.

Comments on Case 7.—One ruminates on one's near-tragedies. Yet it was two years before the histories taken from other patients with acute appendicitis began to evolve in my consciousness the notion that their early symptoms were the same as mine.

CASE 8.—A 24-year-old dental student entered the hospital complaining of suprapubic discomfort of twenty-four hours' duration.

The onset had been gradual, with a "full or stuffed feeling" vaguely referred to the lower abdomen. He volunteered the information that "it felt like gas stopped up inside." He immediately went to the toilet and passed a small, soft stool and a little gas. This partially relieved him. There was no anorexia. He vomited once.

Nine hours later a physician gave a laxative and a shot in the arm and told him he would feel well by morning. This satisfied the patient, who had had several previous brief similar attacks. Marked bowel consciousness and many unsuccessful efforts at defecation; only gas could be passed and the sensation was unrelieved. In the morning the symptoms subsided completely and the patient felt hungry and well.

The temperature was 99.2° F.; the pulse 72; the leucocytes 14,250, later rising to 18,400 with stabs 7 per cent, segments 75 per cent, lymphocytes 10 per cent, and monocytes 8 per cent; the urine normal.

The abdomen was absolutely soft though slightly distended, and rectal and abdominal examination by four different physicians failed to detect tenderness.

Chiefly because of the definite history of gas stoppage, appendectomy was advised. The appendix was found swollen, covered with fibrin, and bound down by adhesions. Histologically acute appendicitis.

Comments on Case 8.—Without the history, volunteered, of gas stoppage, this acutely inflamed appendix would not have been removed promptly, for there was no localization.

CHILDREN

What about children? We have seen so few of them that it does not seem fair to generalize. Some of the children with acute appendicitis proved by operation have eluded our attempts to elicit a story of gas stoppage, others have not. Further observation will be required to establish the reason for this. One case history is presented here. The story was obtained from the child, since the mother's story was misleading.

CASE 9.—A boy, 13 years old, was brought by his mother who said he had headache, fever and eye pains. Present Illness: She said that yesterday he complained of constipation for one day and took a laxative last evening, resulting in two bowel movements. The appetite was good, and there was no vomiting; he slept well last night. This morning on arising complained of headache, eye pain, and photophobia. He took aspirin this morning, attended school. No vomiting, good appetite. There were two bowel movements today. Yesterday evening slight epigastric pain. This has not recurred today. Temperature this afternoon was approximately 101° F. He was subjectively improved this evening. Questionable history of similar attacks before the age of five.

Let us compare this history of the mother's with one taken by a trained observer, Dr. M. M. Cook, directly from the same patient.

Chief Complaint: abdominal pain and fever.

Present Illness: Onset gradual and indefinite about noon yesterday, thirty hours ago, with vague abdominal discomfort which the patient described as an "ache." Not severe, but the patient "felt bad." He felt as if a bowel movement would relieve the distress and he made three unsuccessful trips to the toilet. Later, on his own initiative, he took a laxative (Ex-Lax), and several hours later had one small semisoft stool with some transient relief. He ate poorly at supper, slept all night. He awoke with some vague abdominal discomfort, not well localized but generally low in the umbilical. He had a headache and his "eyes burned." He took aspirin and went to school after a very meager breakfast of a slice of toast and water. He marched in the school parade and became very fatigued. He returned home, felt "very bad," took his own temperature (102° F.), and went to bed. There was dysphagia but not nausea. There is a history of several somewhat similar previous attacks, none this severe. No genitourinary symptoms. He had mild nasal congestion for several days, but no other upper respiratory symptoms.

Examination showed temperature 101.8° F.; pulse 80; leucocytes 7,000 with basophiles 2 per cent, eosinophiles 2 per cent, stabs 20 per cent, polymorphonuclears 60 per cent, lymphocytes 16 per cent. Face very flushed, with circumoral pallor. Jaws seemed full but there was no definite parotid or lymph node enlargement. Nasal mucosa was congested and the pharfynx red. The abdomen was flat with a moderate tenderness in both upper and lower quadrants, and rebound tenderness. Marked tenderness on the right by rectal examination. Diagnosis: appendicitis. Appendec-

tomy was done the next morning, the appendix lying at the level of the umbilicus, with adhesions causing angulation, and a fecalith at the kink, with distal swelling. The peritoneal cavity contained increased clear fluid. Histologically subacute appendicitis.

Comments on Case 9.—Without the direct history from this 13-year-old boy the diagnosis would have been delayed, perhaps missed, because of the upper respiratory infection and poor localization. He answered the three questions Yes, Yes, No. The gas stoppage sensation established the diagnosis which otherwise was uncertain. The history as given by the mother was misleading.

DIAGNOSIS AFTER THE ATTACK

CASE 10.—A 20-year-old married woman was referred with the diagnosis of appendicitis because of two attacks within the preceding three weeks. Both attacks had lasted three days and had begun gradually with dull epigastric heaviness which she attributed to something she had eaten. She answered the three questions relative to gas stoppage sensation at onset, Yes, Yes, no. After onset she went to bed, and took a laxative. There was no nausea or vomiting. The bowels moved but without relief of the abdominal discomfort. There was anorexia, but no vomiting. After about twenty-four hours of discomfort of this type, pain localized in the right lower quadrant. There were no menstrual irregularities. She called a physician who diagnosed appendicitis and "froze it out." She spent three days in bed. A consultant recommended operation, for which she came to me. She was in the interval between attacks, with tenderness at McBurney's point the only positive finding. The leucocyte count was 8,800.

I found a more acutely inflamed appendix then expected, it being so friable that it ruptured during removal. Histologically subacute appendicitis.

Comments on Case 10.—The sensation facilitated the diagnosis of recurring acute appendicitis.

COMMENTS ON THE TEN PATIENTS IN GENERAL

The striking feature of the sensation of gas stoppage, as described by these patients, is the variety of names they spontaneously chose for it. Only one patient (Case 3) spoke of pain but since he also called it "a dull soreness," "a griping," and in answer to a question, "I can't describe it," the pain was certainly vague. Those who stuck to a single term said "gas stoppage," "cramps" or "griping" (three patients), "distress," "dull ache," "heaviness," "gas stopped inside," or "a stuffed feeling." I felt a "tugging," a "pulling on my mesentery." The patient reported as Case 6 felt "cramps," "a tight feeling," "not exactly a pain but a gnawing."

In contrast, in answer to question 1, every one of them accepted a "sensation of gas stoppage" as a precise description of what they felt.

Patients reported as Cases 2 and 4 noticed the feeling of gas stoppage during the onset but only some hours after the first discomfort began.

The discomfort at onset was always in the midline. Four patients spoke of the discomfort as generalized, four located it in the epigas-

trium, and one in the hypogastrium. The discomfort of the first patient moved from the hypogastrium to the epigastrium.

Note how real to the patient is the sensation of gas stoppage. Without cathartic or enema eight of the patients could not pass gas, six could not pass feces, and some of them struggled to do so (Case 4). Yet to the surgeon the gas stoppage remains a symptom, not a sign. It is an ineffective cramp. It disappears as localization occurs or when the appendix is removed.

Table I tells the rest of the tale. Note that five of the patients denied nausea and vomiting. Under prevailing methods of diagnosis the absence of these classical symptoms helps confuse the diagnosis. Equally confusing was the fact that localization was typical in only one-half the patients. (No statistical deduction is to be drawn from this; the cases were selected and are, in any case, too few.)

GAS STOPPAGE AT ONSET OF OTHER CONDITIONS

A. Present.—At onset most patients with acute intestinal obstruction show for a brief time clear-cut gas stoppage not distinguishable from that of acute appendicitis.[1] But this period is brief. Soon nausea and vomiting dominate the scene and localization occurs at the site of obstruction (for example, strangulated hernia).

One patient with terminal ileitis, without obstruction, and with inflammatory changes extending to the appendix, at onset had a sensation of gas stoppage. Similar early symptoms caused me to miss the diagnosis of a patient whose small intestine had been perforated by a toothpick.

B. Absent.—

CASE 11.—Perforated peptic ulcer. At 2:30 P.M. a young woman entered the hospital complaining of very severe abdominal pain.

Suddenly four hours previously she had felt a sharp pain on the left side over the fifth and sixth ribs. Previous attacks of similar pain had been diagnosed as pleurisy. The pain was severe, steady, not colicky. It "almost took her breath away"; she thought it was a heart attack. It radiated to the precordium and to the left shoulder but soon localized in the epigastrium. She found relief by lying on her right side. She tried to belch and took an alkali powder. She did not think of taking a laxative and did not go to the toilet. No nausea or vomiting.

She answered the two questions, Yes, Yes. But after consideration she answered the second question, No. In the end she said that belching rather than passing gas was what she felt would relieve her pain. Therefore, the sensation was absent.

The patient's actions, as usual, spoke louder than words. She took an alkali, not a cathartic. She made no attempt at passing gas or stool.

Actually the diagnosis was never in doubt. Physical signs pointed to a perforated peptic ulcer; x-ray with the patient in the upright position showed free air under the diaphragm.

CASE 12.—Acute cholecystitis. A 75-year-old man, complaining of severe abdominal pain, was sent to the hospital; diagnosed, acute appendicitis.

Onset sudden at 9 P.M. the night before, after retiring. The pain felt "like a boil underneath there," the patient pointing just beneath the right nipple, with a "pulling this way," pointing to the epigastrium.

The pain, then, was definite. By morning it had worked down to a point one inch above the right anterosuperior spine somewhat posteriorly. It felt "like a bag of potatoes." For relief he went once to the toilet but he effort to pass gas or to have a movement was in vain. Then he vainly tried to vomit. He took a laxative and made no further efforts at stool until a normal movement the next morning. This did not relieve the pain.

No nausea or vomiting. No previous attacks.

He answered the question, Yes, No, No. He felt that relief might have been had by passing gas upward. Therefore, the sensation was absent.

A ruptured gall bladder was found at operation.

CASE 13.—Ruptured ectopic gestation. The patient, a 37-year-old woman, had been married ten years and was childless. No menstrual irregularities before admission.

Ten days previously, while working in a store, she felt nauseated. Shortly thereafter there was sudden, definite pain in the right lower quadrant which lasted one hour, then disappeared completely. (The last menstrual period had been a week before this and normal, but there had been a little spotting just before onset.) After the pain disappeared, the patient felt as usual for ten days and kept on working. Then the spotting, nausea, and sudden pain recurred. This time the pain became steadily worse and rapidly incapacitating, and nine hours later the patient was brought to the hospital in an ambulance.

Questions 1 and 2 were answered, Yes, Yes, but this feeling lasted no more than an hour. The pain was not in the midline, as it should have been at the time of a real appendical gas stoppage. The pain was sharp and had been preceded by nausea and spotting on two occasions.

She was referred to a gynecologist who found at operation a ruptured ectopic pregnancy on the right side and dermoid cysts of both ovaries.

CONCLUDING REMARKS

The surgeon who finds time to sit by the bedside and listen to a patient's vague, rambling story of the onset of an attack of acute appendicitis (and then aim at the heart of it with his three questions) will discover that the words quoted in this paper by no means cover the names a man can call a cramp in his middle. And if the surgeon is interested to study how movements (inward or outward), position, digestion, atmosphere (smoky), etc. aggravate or do not aggravate the discomfort at onset, he has a job cut out for him—and after such study doubtless the surgeon will have a name for it himself.

The writer of a clinical paper is inevitably indebted to the bedside battles that have clarified his notions for him. Many discussions in the Student Health Clinic satisfied Dr. M. M. Cook and me that the phrase "bowel consciousness," suggested by him, best expresses the patients' sensations, but the patients themselves proved to us that "sensation of gas stoppage" says something to them.

How different the second pain, the pain of localization! This is as precise as the onset discomfort is vague: precise in time of onset,

precise in situation, precise in quality; "it feels like a boil," "like a toothache," "a real pain," "right there."

What we have called the sensation of gas stoppage occurs during the onset (and only during the onset) of acute appendicitis, prior to "localization." Studies in progress since a former paper was published in February, 1944,[1] suggest that the sensation of gas stoppage is present during the onset of forty out of fifty proved cases. Sufficient experience has not accumulated to warrant a more specific statement.

But this may be said: The patients from whom we have failed to get a convincing story are (a) children, (b) patients with a low I.Q., and (c) patients who begin their attack in mid-career, as it were, with the pain of localization and without the brief, vague onset period that has been so repeatedly described in these pages. It seems, up to the moment, that the more fulminating cases (for example, Case 4) tend to exhibit the clearest picture of gas stoppage. Should further experience confirm this hint, study of the onset symptoms will indeed be worth the surgeon's while.

And what conditions other than acute appendicitis show at onset the symptoms of gas stoppage? Notably small intestinal obstruction and other less usual diseases of the small intestine.

What, then, of errors resulting from this attempt to establish a diagnosis of acute appendicitis before localization? There have been errors enough but all they have taught us is to study the early history of the attack more precisely and ever more precisely. The cases cited hint at some of the difficulties encountered.

The battle of the bedside! One questions, sometimes, whether the triumphs of the operating room impart so fierce a joy! Let us not forget, when pressed, that at the battle of the bedside the patient is on our side, if we happen to be right.

The suggestions herein contained will not make the battle of the bedside any less sharp. Nor will the acceptance of the patient's onset history as part criterion for the diagnosis of acute appendicitis, in a sense, make this diagnosis any easier. It is a long, tedious job to take a good history.

SUMMARY

1. A vague midline sensation of gas stoppage characterizes the onset of acute appendicitis.

2. It induces the patient (a) to seek the toilet (b) to take laxatives.

3. During the time of onset, a period from one to more than twenty-four hours, few patients are able to pass gas or to defecate without catharsis or enemas. Those able to pass gas or to defecate obtain little or no relief thereby. Hence, the sensation is a symptom and not a physical sign.

4. This bowel consciousness is an urge downward rather than an upward urge of nausea or vomiting.

5. The sensation of gas stoppage ends when pain localizes over the appendix, usually in the right iliac fossa. The features described are then altered. There is a definite pain which is different.

6. The gas stoppage sensation is present at onset irrespective of whether localization later is "typical," "atypical," or absent.

7. The sensation is particularly valuable in fulminating cases.

8. Three questions have been devised to elicit it. To find it, the examiner should carefully focus the patient's mind on the time prior to localization of pain, to the time not when he first felt sick, but when he last felt perfectly well.

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UROLOGIC PROBLEMS ASSOCIATED WITH THE SURGICAL TREATMENT OF CARCINOMA OF THE RECTUM

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I PURPOSE to discuss the urologic problems involved in the surgical management of cases of carcinoma of the rectum under three categories, namely, (1) the problem of urinary retention, (2) the problem of urosepsis, and (3) injuries of the ureter, urethra, and urinary bladder.

URINARY RETENTION

Urinary retention which may follow the Miles or Kraske operations, and their modifications, for carcinoma of the rectum is probably one of the most frequent complications consequent upon radical surgery for this disease. Despite considerable study, the cause of this complication is as yet incompletely understood. Complete emptying of the bladder depends, to a great extent, upon the functional adequacy of the detrusor muscle, which in turn is dependent upon the condition of its major motor nerve supply from the parasympathetic fibers of sacral roots 2, 3, and 4. The usual explanation of vesical atony which follows the radical operation for carcinoma of the rectum is that a certain degree of trauma is inflicted upon these nerves during the course of the surgical procedure. However, according to the experimental work of Coller and Eastman, this explanation is entirely inadequate. The investigators studied the motor activity and thermal sensation before and after operation in twenty-two unselected cases. Presurgical cystometric readings among normal persons disclosed a large range of variations in bladder capacity and intravesical pressure. A similar set of readings taken after operation failed to show any variation which would tend to indicate injury to nerves governing vesical function. Although five patients developed temporary urinary retention, the underlying cause could not be ascertained, even though it was believed that temporary edema of the urethra incident to surgical trauma played a role in two patients. Another hypothesis which was advanced was that retention might have resulted from division of the sacrovesical ligament, thereby leading to distortion of the part of urethra lying between the vesical neck and the membranous urethra, which was sufficient to cause mechanical obstruction.

Urinary retention has been known to follow hemorrhoidectomy or hernioplasty, where the possibility of injury to the vesical nerve supply could be definitely eliminated. This phenomenon has never been adequately explained. It is my impression that disturbances in urination which frequently follow the radical operation for carcinoma of the

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rectum are due to both factors, namely, injury of the extrinsic nerve supply of the urinary bladder, and interference with the normal supportive structures of the bladder neck and posterior urethra.

Urinary retention usually follows immediately on completion of the surgical procedure and, unlike retention which so frequently complicates most operations, it may persist for days, weeks, or on some occasions even months. Failure of the bladder to expel urine responds to one type of treatment or another, only to recur at some later date.

Paradoxical incontinence is not an unusual manifestation in some of these cases, especially in the later phases of convalescence, and frequently requires the use of mechanical devices designed to prevent soiling of clothing.

The presence of varying amounts of residuum may persist for long periods following operation, even though patients may urinate with no apparent difficulty. In women procidentia frequently aggravates the condition, while in men the presence of enlarged prostates may intensify the difficulty.

Prevention.—Probably the most important problem associated with the prevention of urinary retention in this group of surgical cases is recognition and correction of conditions which are actively causing, or which can give rise to, obstructive uropathies. It seems to me in the light of my experience that a woman with a well-defined cystocele, particularly when associated with urinary retention, should have a perineorrhaphy performed before undergoing the radical operation for rectal carcinoma. This view is, admittedly, not that of many eminent surgeons. In male patients, every effort should be made to elicit pertinent and precise information regarding urinary difficulties. In the event the patient presents suggestive symptoms, a thorough cystourethroscopic study of the vesical neck and posterior urethra is indicated. Should the examination disclose an obstructing prostate, a median bar, or vesical neck contracture, experience has dictated to me that appropriate measures must be carried out to correct them before intestinal surgery is undertaken. Again, it seems to me that transurethral resection, wherever possible, is the procedure of choice, and can be expeditiously performed a few weeks prior to the intestinal resection. This is a purely personal view of the matter, which is hardly shared by surgeons in general.

The presence of urinary residue which cannot be accounted for by an obstructing lesion warrants a complete neurologic investigation and cystometric study. Attempts at correcting or improving atony of the vesical detrusor by cholinergic drugs such as doryl, furmethide, or others should be made prior to operation. Failure to obtain improvement warrants the performance of suprapubic cystostomy immediately following the radical operation for carcinoma of the rectum.

I believe a procedure well worth trying as an aid in preventing impairment of vesical function subsequent to surgery is the introduc-

tion of an indwelling urethral catheter for continuous tidal drainage immediately before the operation, to be left in situ during the course of the operation and for a week or ten days after.

Gentle and careful handling of tissues during the perineal phase of the operation, especially during the stage of separation of the rectum from the bladder, will greatly minimize the risk of this complication. Another important factor in preventing postsurgical vesical atony is proper packing of the perineal wound following extirpation of the rectum, in order to give ample support to the bladder neck during the early stages of convalescence.

Treatment.—The active treatment of acute or subacute urinary retention occurring during the convalescence from radical surgical removal of carcinoma of the rectum consists in tidal drainage for at least ten days following the onset of symptoms. Should the procedure fail to restore full vesical function, cholinergic drugs may be tried along with measures designed to cause the expulsion of urine from the atonic bladder through manual abdominal wall massage carried out at regular stated intervals, as is employed in treating those afflicted with other varieties of neurogenic bladder disturbances.

It has been my experience that most patients with urinary retention eventually respond to conservative treatment. Before discharging a patient as cured, it is necessary to ascertain whether or not the bladder empties completely after voiding. Since the tendency toward recurrence of urinary retention in this group of patients is not infrequent, it is advisable to have them return at least every four months in order to determine the amount of residuum present. Excellent results often follow the method of gently overdistending the bladder with a 2 per cent solution of boric acid once or twice weekly.

In the event obstructive uropathies have been overlooked or had not been removed prior to operation, prompt corrective measures should be undertaken following the onset of symptoms which suggest vesical dysfunction. It is obvious that careful cystourethroscopic studies are of the utmost importance before the institution of corrective therapy.

UROSEPSIS

Urosepsis is a complication which must be assiduously watched for in all patients subjected to radical operations for carcinoma of the rectum. This complication is more or less dependent upon a variety of conditions, some of which antedate the surgical procedure, and others which follow. It is of the utmost importance for any surgeon contemplating a radical operation for carcinoma of the rectum to ascertain the exact status of the urogenital tract. Among the more common conditions predisposing to postsurgical urosepsis are (1) the presence of obstructive uropathies such as vesical neck obstruction from hypertrophic prostates or median bars in men, and cystoceles in women; (2) active infections within the prostate, bladder, or upper

urinary tract; and (3) spreading infection from an ulcerating carcinoma of the rectum to the bladder by way of the regional lymphatics or by direct extension.

The most important factor in the etiology of urosepsis following radical surgery for carcinoma of the rectum is the loss or impairment of expulsive power of the detrusor muscle, leading to urinary stasis. Another causative factor, although of less importance, is the hazard involved in frequent catheterization of patients with atonic bladders. Patients with carcinoma of the rectum have a lowered resistance to all varieties of infection, and are in many respects comparable to patients with neurogenic bladders following transverse myelitis of the cord, where resort to frequent catheterization is definitely contraindicated.

Following extirpation of the rectum, a large cavity results which lies adjacent to the posterior vesical wall. This cavity, in a large percentage of patients, becomes infected immediately following the surgical procedure, or shortly after. I believe that this eventually leads to pericystitis, and is therefore another important cause of postsurgical urosepsis.

Prevention.—The prevention of urosepsis in these patients depends upon its detection prior to operation, and upon the recognition of conditions within the urogenital tract which have a predisposing tendency to infection. It is obvious that in order to discover infection or predisposing factors that may lead to infection, it is necessary to subject the patient to a thorough investigation of the genitourinary system prior to operation. This requires a complete cystourethroscopic examination, pyelography, and bacteriologic study of the segregated urines. Correction of factors predisposing to infection, such as obstructive lesions anywhere along the genitourinary tract, should be accomplished before the colonic operation is performed. Chemotherapy is instituted to control existing infection. Frequent interval examinations of the urine should be made and the emptying capacity of the bladder determined for at least one year following operation, in order to avoid urosepsis which may occur late in the course of postsurgical convalescence.

Treatment.—Urosepsis which develops after operation should be treated along orthodox urologic lines. Chemotherapeutic agents administered orally or parenterally as conditions warrant, accompanied by free urinary drainage, are the prime features in the therapeutic program. In the event that the source of the trouble is in the lower urinary tract, the procedure of choice is tidal drainage through an indwelling urethral catheter, or better still, through a suprapubic cystostomy tube. However, it appears to me, but may be arguable by other surgeons, that if the condition is in the upper urinary tract, ureteral catheter drainage or drainage through a nephrostomy tube may become necessary.

INJURY OF THE URINARY TRACT

Injuries to the genitourinary tract most likely to occur during the course of a radical resection of the rectum are (a) injury of one or both ureters, (b) injury of the bladder, and (c) injury of the urethra. Injury of the ureters may occur during the abdominal stage of an abdominoperineal resection, and less frequently during the perineal stage. The bladder and urethra are liable to be injured during the perineal stage of the operation.

Prevention.—Because of its closer proximity to the pelvic portion of the rectum, the left ureter is more likely to be injured than the right during the abdominal stage of the operation. To minimize this danger, it is advisable, following the re-establishment of the pelvic diaphragm, to inspect the ureters to assure their continuity and patency. Should a ureter be inadvertently injured, immediate repair over a splinting catheter is recommended.

Although the lowermost ends of the ureters may be injured during the perineal stage of the operation, the more likely complication is injury of the bladder or posterior urethra, particularly in male patients. The introduction of a urethral catheter prior to operation will obviate, or at least greatly minimize, this hazard. To reduce the danger of injuring the bladder, good visibility of the surgical field during the abdominal and perineal stages is of the utmost importance. This is particularly true when liberating the rectal part from its anterior and lateral attachments. Another important factor is securing perfect hemostasis in order to avoid blind clamping of bleeders and the use of mass ligatures in a field obscured by excessive bleeding. Clean sharp dissection and the establishment of proper planes of cleavage in separating the rectum from the bladder will greatly minimize this risk. It is also important to recognize the presence of vesical wall infiltration by the tumor, which tends to expose the bladder to accidental injury during the course of dissection. And finally, in the event that the bladder is accidentally opened, it is necessary to close the opening promptly in layers and to introduce an indwelling urethral catheter which should be permitted to remain in situ for a week or ten days after operation.

Treatment.—Postsurgical injuries of the ureter should be treated in the same manner as injuries resulting from any other cause. End-to-end anastamosis of the divided ureter, using a splinting ureteral catheter or T tube, preferably with a complementary nephrostomy, or implantation of the proximal end of the severed ureter into the bladder when feasible, or nephrectomy providing the other kidney had been previously found functionally adequate to maintain life are the procedures generally recommended. It is perhaps needless to state that

the prompt repair of an injured ureter will yield better results and will entail less difficulty in repairing than when left for some later date.

Injuries of the bladder or urethra, like injuries of the ureter, should be repaired immediately. In the bladder, for example, the opening is promptly closed with two layers of fine chromic catgut, avoiding the inclusion of vesical mucosa in the line of sutures. This is to be promptly followed by the introduction of an indwelling urethral catheter which is permitted to remain in place for a week or ten days. The use of sulfonamide drugs is of value here.

The surgical problem becomes much more complex when dealing with repair of vesical fistulas, particularly of the perineal type which usually occur late in the postsurgical course. This is due to the presence of scar tissue which makes it difficult to expose the edges of the fistulous opening, a step essential to successful closure. I have found the use of Young's boomerang needle of inestimable value in the repair of perineovesical fistulas. In the latter type of case I have resorted to a two-stage procedure consisting of a suprapubic cystostomy as the first stage, followed, after a reasonable interval, by perineal closure of the vesical opening. In the interim between the first and second stages, great stress is laid upon proper cleansing of a perineal wound, which is usually grossly infected when the patient first comes under observation, and also upon bolstering the patient's resistance and physical stamina.

During the second stage of the operation the patient is placed in the Sims' position, or prone with thighs depressed. The original perineal wound is enlarged and deepened down to the bladder. All granulations and scar tissue leading down to the fistulous opening in the bladder are excised and the edges of the bladder constituting the mouth of the fistula are freed and inverted with interrupted fine chromic sutures introduced through a Young boomerang needle. To test the accuracy of closure, a small amount of indigo carmine or methylene blue solution is introduced into the bladder through a suprapubic tube in order to see whether any escapes into the perineal wound. The overlying wound is then salted with sulfanilamide crystals and closed in layers. Before removing the suprapubic tube, it must be definitely ascertained that (a) the perineal wound is solidly healed, and (b) the urethra is fully patent. To be assured of the patency of the urethra throughout its entire length, it is necessary to be able to pass freely bougies of reasonable caliber into the bladder.

In repairing defects of the posterior urethra, which is the segment of urethra most likely to be injured during the perineal stage of the operation in male patients, the same fundamental principles hold good as in the repair of injuries of the urethra following other causes. Small openings frequently heal following the use of an indwelling

urethral catheter. When larger parts of the urethra are involved, various plastic procedures can be carried out through fresh incisions in the perineum similar to those employed in perineal prostatectomy. Similar procedures can be performed by reopening the original sacral wound. A preliminary suprapubic cystostomy greatly facilitates healing in this group of patients.

SUMMARY AND CONCLUSIONS

This article deals with the prevention and treatment of the more common urologic complications which may follow the radical operation for carcinoma of the rectum. An attempt has been made to explain the underlying causes of these complications in order to facilitate a more comprehensive understanding of the principles employed in the prevention and management of each complication.

THE CONSERVATIVE AND OPERATIVE TREATMENT OF LESIONS OF THE INTERVERTEBRAL DISCS IN THE LOW BACK

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DURING recent years the conviction is growing that the symptoms which we formerly attributed to sacroiliac or lumbosacral strain, arthritis or subluxation, lumbosacral facet syndrome, postural strains of the low back, and myofascitis or fascitis in the lumbar region are really due to lesions of the intervertebral discs in this area. This is especially true in patients with sciatic pain. These do not include all patients with pain in the back, but are the large group of patients with obscure low back pains with or without sciatica in which the general physical and laboratory examinations and the x-rays revealed no explanation of the symptoms, except possibly a narrowing of one or more intervertebral discs.

For years investigators have sought to explain the symptoms in these low back conditions with the hope that once the pathology was satisfactorily demonstrated it would be possible to formulate a logical therapeutic attack on the lesion and thus treat these patients with confidence, precision, and uniform success.

Now that the pathology is known it seems right and logical to remove the protruding nucleus pulposus and relieve the patient promptly and completely. Unfortunately, this involves a rather difficult major operation and even after this has been done a few patients complain of the same pain and disability and a considerable percentage of them are not completely relieved. In focusing our attention on the protruding disc we are apt to ignore the fact that these lesions occurred just as frequently in the past as they do today and that in the past it was possible for us to relieve the great majority of our patients without operation.

The methods which we used were rest, traction, heat, support to the low back, correction of body mechanics, deep x-ray therapy, manipulations with or without anesthesia, and finally fasciotomy, operative fusion of the sacroiliac joints or the lumbosacral spine, or fusion with resection of the articular facets. We treated the patient conservatively over a considerable period and resorted to surgery only in those instances where prolonged conservative treatment had failed to relieve the pain and disability and where these symptoms were sufficiently severe to warrant a major surgical procedure followed by a prolonged convalescence.

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Now that we know where the pathology lies there is no reason why we should not continue the same general plan with the amendment that we now have something more definite in the field of surgery to offer these patients if prolonged conservative treatment has failed to relieve their symptoms or if circumstances make conservative treatment impractical.

It is to be noted that the severity of the symptoms and the degree of disability vary greatly in different patients and at different times in a given patient. The same is true of the findings on physical and neurologic examination. One patient may complain of a mild pain in the low back which occurs occasionally after prolonged standing or sitting or strenuous exercise and another may be confined to bed with a severe pain in the low back which radiates down the back of the thigh and leg to the foot and is lessened but not relieved by certain postures, but becomes agonizing with the slightest movement.

In the first patient the physical examination may reveal nothing abnormal and in the second patient pain may prevent a satisfactory examination. It is also to be noted that the mild symptoms may become severe after a strain of the low back or without known cause and the severe symptoms may subside with or without treatment. It is thus understandable why many patients give a history of previous attacks. A condition which is characterized by recurrences must also be characterized by remissions.

Our assumption that the mild low back pain and the severe pain with sciatica, and all gradations between the two extremes, are due to lesions of the intervertebral discs in the lower lumbar region is based on the operative finding of these lesions in the more severe cases and the repeated clinical observation that not only are all gradations between the mild and the severe cases seen in different patients, but the progression or regression of signs and symptoms may be observed in a single patient.

Study of a series of patients suggests that the low back pain may be due to the lesion in the annulus fibrosus or a midline protrusion and the sciatic pain to irritation of a nerve root by a lateral protrusion of the disc.

In planning the treatment of these patients it is necessary to adapt the treatment to the patient and his symptoms. In the great majority of instances the patient is able to continue his or her normal occupation and is treated as an office patient. In others change of occupation is necessary. In the presence of severe pain and disability, rest in bed is advisable until the pain subsides or is relieved. Operation is reserved for those who do not respond to conservative treatment and who are sufficiently disabled to render operation justifiable and to those in whom prolonged conservative treatment is not practical. We can thus divide the patients into three groups: the ambulant, bed, and operative groups.

The diagnosis is made and the type of treatment indicated for a given patient is determined from the history and physical examination. In many cases the history is more important than the physical examination This is because the findings on physical examination depend largely upon the severity of the symptoms present at that time and these may vary from day to day, and even from hour to hour. Frequently, a patient with a suggestive history is asked to return for a second examination when pain is present after exercise, prolonged standing, or whatever aggravates the pain in this particular patient. This is especially true with a history of prolonged disability which has not been relieved by conservative treatment and where operative treatment is being considered.

Routine x-rays of the lumbosacral region are made to rule out disease or spondylolisthesis or to note congenital anomalies, if present. In cases of long duration the x-ray may supply confirmatory evidence of an intervertebral disc lesion, as the space between the bodies of two vertebrae may be narrowed. But it is to be noted that even in these instances the symptoms may arise from a neighboring disc which presents a normal appearance in the x-ray.

No laboratory examinations or elaborate medical surveys are necessary before beginning treatment of the average patient. These patients are normal individuals who have a low back strain. Before operation they should have a general physical examination, just as should any other patient who is to be subjected to a major surgical operation.

Spinograms are not done. If the patient is to be treated conservatively the exact location of the lesion is of no importance. If he is to be operated upon the location of the point of tenderness in the back directly over the lesion, the distribution of the pain, and the neurologic findings enable an experienced clinician to localize the lesion as accurately as can be done in the spinogram. In addition, many surgeons routinely explore two discs at operation.

Treatment of Ambulant Patients.—Ambulant patients are treated by support to the low back, manipulation, stretching of the low back, and correction of body mechanics by exercise, a hard flat bed, vitamin B, weight correction and salicylates, and change of occupation if necessary.

A support which tends to flatten and immobilize the low back is prescribed for practically all of these patients. The women are given a corset or girdle which grasps the pelvis and extends up to about the tenth dorsal vertebra. This has stays up the back and can be laced or strapped tightly around the body. Men are given a wide canvas belt of about the same dimensions which has stays but no pad in the back and straps or lacing in front. The belt is narrowed in front to permit sitting (Fig. 1). Many patients when first examined are wearing a narrow canvas sacroiliac belt with a pad. These are less efficient than

the wide belt and are discarded. When more rigid support is needed a signet ring plaster of Paris jacket or belt is applied. This is wide behind, extending from about the tenth dorsal vertebra to the lower sacrum and is narrow in front, being shaped like a signet ring. It is applied with the lumbar spine flat or flexed. The patient grasps an iron upright, places his feet against its base and sags backward, retracting his abdomen while the plaster is being applied. After it has hardened the plaster is trimmed in front to permit sitting and bending.

If immediate support is indicated for acute symptoms the back is strapped with adhesive. The patient lies prone with a pillow under his abdomen, and the cross strapping begins at the midaxillary line at the level of the trochanter and extends up to grasp the lower two or three ribs. This is worn for about ten days, or until a removable support is obtained.

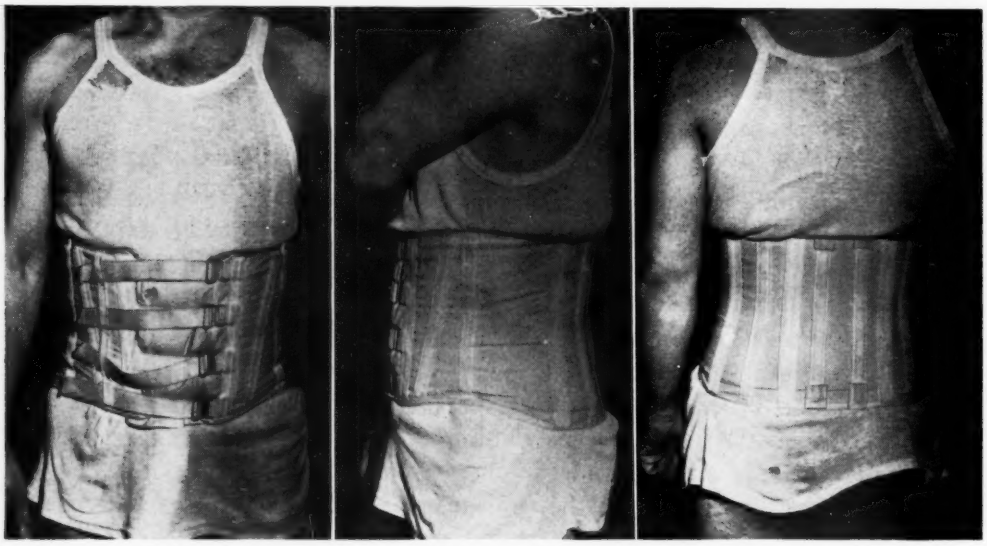

Fig. 1.—Lumbosacral belt as used for low back pain. (Three views.)

Manipulation.—The object of the manipulation is to widen the space between the posterior parts of the bodies of the vertebra and thus cause retraction of the disc. Only three maneuvers are used routinely. The patient lies on the unaffected side facing the surgeon with the upper (affected) leg hanging over the side of the table. The surgeon grasps the patient's shoulder with one hand and places his opposite forearm on the crest of the ilium. When the patient is relaxed the surgeon delivers a quick thrust and pushes the ilium down and forward while the shoulder is pushed up and back. This movement may produce a crunching sound and frighten the patient, but rarely causes pain. The manipulation is repeated on the opposite side and the patient is then turned on his back and both knees are strongly flexed on the abdomen, thus flexing the lumbar spine. These manipulations may be followed

by a variable amount of relief or they may be ineffective. The back may be strapped with adhesive after the manipulation.

Body Mechanics.—The patient is taught to sit, stand, and walk with the head up, chin in, chest up, abdomen in, back flat, and hips in. He is also given exercises to strengthen the abdominal, back, gluteal, and lower extremity muscles and to flex and stretch the lumbar spine and elevate the diaphragm.

Bed.—A piece of plywood cut to fit over the springs or boards placed lengthwise are put between the mattress and the springs and a firm mattress is advised. This is not insisted upon if, after a fair trial, the patient is more comfortable in an ordinary bed.

The patient's diet is regulated in an effort to cause his weight to approach the normal for his age and type. He is given about six times the daily requirement of vitamin B complex. This has a tonic effect, gives most patients a sense of well-being and makes them feel better. If the pain is sufficiently troublesome the patient is given aspirin or some other form of salicylate and, rarely, small dose of codeine, or he may use local heat to the low back at night for pain. He is advised to avoid heavy lifting, stooping, prolonged standing, or whatever seems to him to aggravate the pain.

As the symptoms subside this regime is gradually discontinued.

Treatment of Bed Patients.—Bed patients are those in whom the symptoms are so severe that they are not able to carry on their daily routine; rest in bed is advisable and is an important part of the treatment. They should be hospitalized, but most of them either cannot get a bed in a hospital immediately or do not want to go to a hospital, so they must be treated at home. They are advised to place boards between the spring and the mattress and to remain in bed most of the time, lying on the back with large pillows under the head and knees or on the unaffected side with the hips and knees flexed (in order to maintain flexion of the lumbar spine). Local heat, either dry or as hot fomentations, is applied to the low back and the patient is instructed to get in a tub of hot water once or twice a day and when relaxed to flex the knees strongly on the chest, thus stretching the lumbar spine in flexion. The local heat and hot bath are omitted if the back has been strapped with adhesive.

Codeine and aspirin are given every four hours for pain and the manipulations described may be used; if necessary, morphine may be given before the manipulation in order to secure relaxation.

If the patient is hospitalized he is kept in bed and is denied bathroom privileges. The manipulation may be performed under avertin or general anesthesia and when this is done forcible straight leg raising, hyperextension of the hips, and strong traction obtained by suddenly jerking the leg downward are added to the maneuvers described.

As the acute symptoms subside the patient is given exercises to strengthen the abdominal muscles, flex the lumbar spine, and correct his body mechanics. He is gotten up gradually with support to the low back and is permitted to resume his normal activities as the symptoms subside. The ambulatory treatment is then continued until the patient is free of symptoms or until operative treatment is advised and accepted. No effort is made to keep the patient in bed until the symptoms are completely relieved, because experience has shown that prolonged rest in bed rarely cures a lesion of the intervertebral disc.

In some clinics injections of novocain into the painful areas are used and reports in the literature indicate that this form of treatment gives permanent relief in a high percentage of the patients. I have tried the method, but with indifferent success, perhaps because I used it only in patients who did not respond to the methods mentioned previously. The same is true of prolonged traction in bed.

If persisted in over a reasonable period the procedures mentioned will result in relief in a high percentage of the patients (probably about 90 per cent) and most of these will be able to return to their former occupations and remain free from symptoms. It is to be noted, however, that some of these patients may have recurrence of the symptoms, either spontaneously or following strain of the low back. The only conservative methods of preventing these recurrences are the avoidance of strain and the maintenance of good posture, and these are not always effective.

Treatment by Operation.—If conservative treatment is unsatisfactory, the patient is not relieved or is intolerant of his symptoms and demands relief by surgery, or if he has a long history of disability which has not responded to treatment elsewhere, operative treatment should be considered.

The operation consists of removal of the protruding disc with or without curettement of the nucleus pulposus and with or without fusion of the spine in the involved area. The operative technique varies widely among different surgeons and if the best results are to be obtained it should be performed by a surgeon who has had considerable experience in this field or who has visited other clinics and observed the technique of surgeons who have had this experience.

The operation may be relatively simple, as the extruded disc may present itself immediately beneath the ligamentum flavum and the nerve root can be retracted and the protruding disc lifted out. On the other hand, the surgeon may encounter profuse bleeding from the extradural veins and have considerable difficulty in controlling this to a point where he can make a satisfactory examination of the disc; then he may have difficulty in deciding whether he is dealing with a normal disc or a hidden disc, as described by Dandy.[1]

Operative Technique.—The technique is as follows: The patient is placed in the prone position with a pillow under the lower abdomen and

the hips moderately flexed to flatten the lumbar spine. A pad is placed under the unaffected side of the pelvis to tilt the back of the patient toward the surgeon who stands on the affected side.

The operation can be performed under general or local anesthesia (1 per cent novocain for the skin and the nerve roots and ½ per cent for the other tissues). The novocain contains 4 drops of adrenalin to the ounce. Preoperative medication consists of 3 gr. of nembutal and ⅙ or ¼ gr. of morphine when local anesthesia is used.

The skin and subcutaneous tissues are infiltrated with novocain and a straight incision extending from about the third lumbar to the second sacral spine is carried down to the spinous processes. The bleeding is controlled. The tissues on either side of the spinous processes are infiltrated and then the needle is directed outward to the vicinity of the articular facets and lamina and the deep tissues are infiltrated on the affected side. Skin towels are applied and with a knife and a sharp chisel and periosteal elevator the spinous processes of the fourth and fifth lumbar vertebrae are exposed subperiosteally. On the affected side the tissues are stripped from the lamina and the sacrum well out to expose the articular facets and a self-retaining retractor is inserted. With a large curette and a sponge the ligamenta flava between the fourth and fifth lumbar and the fifth lumbar and the first sacral vertebrae are cleaned of the fat tissue which lies over them. At this point the spinous processes are grasped with a heavy toothed artery clamp and manipulated up and down in the horizontal plane or are pushed upon with an osteotome in order to demonstrate any abnormal mobility. Dandy considers abnormal mobility of the spinous process a pathognomonic sign of an abnormal intervertebral disc. I consider it confirmatory evidence, but rely more on the history and physical examination of the patient and visual examination and palpation of the disc. Likewise, I have not always been successful in identifying the ruptured disc by pressure on the ligamentum flavum. If the nerve root is pushed back against the ligament the pressure will cause sciatic pain, but in many instances the nerve root is some distance anterior to the ligament and in these pressure on the ligament does not cause pain.

If a lesion of the lumbosacral disc is suspected the ligamentum flavum is separated from the deep surface of the inferior margin of the lamina of the fifth lumbar vertebra with a thin curved periosteal elevator or chisel. A good-sized button of bone comprising about one-half of the width of the lamina and extending as far laterally as possible is removed with a rongeur.

It is possible to remove many discs without removing any bone and I have done so, but have discontinued the practice because a much more satisfactory operation can be performed and the bleeding controlled more effectively if an adequate exposure is obtained in the beginning. And the removal of the button of bone from the lamina does no harm. A

similar button of bone may be removed from the superior margin of the sacrum if necessary.

The ligamentum flavum is then nicked with a small knife, care being taken not to incise the dura. It is grasped with an artery clamp and excised as completely as possible in one piece. Any remaining tags of the ligamentum flavum which may obstruct a clear view of the disc are also excised. The extradural fat is retracted or picked out to expose the nerve root and this is injected with about ½ c.c. of 1 per cent novocain. The nerve root is very sensitive and even when the injection is done with a very fine needle on a tuberculin syringe this may cause a severe pain down the patient's leg. This is almost the only pain suffered by the patient after the initial infiltration of the skin. The nerve root is usually injected through the ligamentum flavum as soon as this structure is cleaned off, but this is not always successful.

It is during or after the removal of the ligamentum flavum that the intraspinal bleeding is encountered and a sucker is necessary to remove the blood from the field. The bleeding is controlled by cottonoid sponges wet with normal saline solution which are packed against the bleeding points and sucked dry with the sucker. These sponges are of two types: (1) strips about one-half inch wide and six inches long and (2) small squares about three-fourths inch across which have a black thread about twelve inches long sewn and tied in the center to prevent loss in the wound. Care is taken not to rupture the thin-walled extradural veins, the largest of which lie near the lateral wall of the spinal canal, but frequently this happens and the surgeon may be working in a pool of blood with a questionable protruding disc in the bottom of the pool, unless he has learned to control this bleeding by suction and packing. I have not used the electric cautery inside the canal for fear of injuring the nerve root.

The surgeon holds the sucker in his left hand and manipulates the cottonoid sponges or a small spatula or blunt dissector with his right. An assistant may retract the nerve root toward the midline with a narrow retractor or the surgeon may hold it over with the tip of the sucker to expose the protruding disc beneath it. In many instances the nerve root is firmly adherent to the protruding disc and must be dissected free before the nucleus can be removed. Usually this can be done by blunt dissection with a small spatula or blunt dissector. The dura may be torn during this procedure and some spinal fluid may escape. I have not tried to suture these small tears in the dura and have not noted any bad effects afterward. If troublesome, they may be closed with a bit of crushed muscle.

In other instances the nerve root is not adherent and is easily pushed aside to expose a glistening disc which is bulging slightly or markedly, but which is not ruptured. When this is pressed upon by a blunt instrument it is found to be compressible or like rubber. This is the concealed

disc described by Dandy. The normal disc is flat and quite firm on pressure, especially when the lumbar spine is flexed.

If the disc is ruptured and extruded the nerve root is retracted toward the midline and the extruded material is removed with a clamp or forceps to expose the cavity beneath. This cavity is then curetted lightly with a medium-sized curette in an effort to remove as much as possible of the nucleus pulposus and thus prevent a recurrence of the protrusion. In using a curette or forceps in the cavity of the disc, care is taken to introduce the instrument gently and not push it in forcibly, as it is possible to penetrate the anterior ligament and injure the aorta. Moderate force may be used in curetting the surface of the vertebral bodies and in pulling the curette out. However, no effort is made to break through the plate of cartilage and bone and expose the underlying cancellous bone with the expectation that the bodies of the vertebrae will then fuse. As a matter of fact, perforation of this plate is avoided.

If the disc is not ruptured a rather large window is cut in its protruding surface, using a tenotome or a urethral knife and, after the loose material is pulled out with forceps, the disc is curetted lightly and an effort is made to remove as much of the nuclear material as possible.

Unless the surgeon is fairly well satisfied that only one disc is causing symptoms, the adjacent disc is exposed and examined and treated in the same manner if it is found to be abnormal. If the first disc exposed is found to be normal the adjacent disc is exposed and examined as a routine procedure and is removed if it is found to be abnormal. If the two lower discs are normal the one between the third and fourth lumbar vertebrae is exposed and examined and removed if it is abnormal. This is apt to be the site of the lesion if the patient has had pain in the groin or anteromesial aspect of the thigh.

Occasionally, in older patients with symptoms of long duration the disc has become obliterated and a ridge of bone is present along the margin of the vertebral body beneath the nerve root. When this is found the nerve root is retracted medially and the ridge of bone is removed with a small thin osteotome, care being taken not to leave any loose fragments in the spinal canal.

The pillow is then removed from beneath the patient's abdomen and the table is straightened. This lessens the pressure in the extradural veins and at this time any cottonoid sponges which are still in the wound are removed. Usually it will be found that there is no further bleeding. However, if bleeding continues the bleeding point is packed off with a cottonoid sponge and a small bit of muscle is cut from the side of the wound, crushed with forceps, and held against the bleeding point until the hemorrhage is controlled and the wound is closed with this muscle in place.

The nerve root is again retracted and the disc inspected. If the change in position has caused any more disc material to appear in the

cavity this is removed. The wound is then sprinkled with sulfonamide powder and closed in layers, using chromic and plain catgut for the deeper tissues and cotton for the skin. A rather small dressing is applied and the patient is placed on an ordinary bed and permitted to lie in whatever position is most comfortable. The skin sutures are removed on the seventh day and he is allowed up on about the twelfth day and permitted to leave the hospital. He is advised to increase his activities gradually and to avoid strain on the back for at least eight weeks.

Spinal Fusion.—If spinal fusion is decided upon, this is done as follows: The deeper tissues on the opposite side and an area over the posterior part of the crest of the ilium are infiltrated with novocain; the lamina and articular facets on the opposite side are exposed subperiosteally. The interspinous ligaments and the periosteum are completely removed from the opposing borders of the spinous processes and lamina and with a rongeur a small notch of bone is pinched out from the opposing borders of the bases of the spinous processes. Small slivers of bone are raised, but not detached from the laminae and posterior surface of the sacrum, and the cartilage is removed from the articular facets.

Through a curved incision over the crest the posterior surface of the ilium is exposed, a rectangle about 1 by 1½ inches is outlined with an osteotome, and the slab of cortex with some of the underlying cancellous bone is excised. A small notch is pinched out of each of the longer sides of this rectangle of bone with a rongeur, the spinous processes are separated by flexing the lumbar spine, and the graft is inserted between them, the notches in the graft fitting in those in the spinous processes. As the lumbar spine is extended the graft is held firmly in place and closely applied to the roughened lamina and sacrum, covering the defect left by the removal of the ligamentum flavum. Additional cancellous bone may then be obtained from the ilium, placed where indicated, and the wound closed. This method results in a rapid fusion and the patient remains in bed without immobilization for three weeks. He then may be gotten up with a wide lumbosacral belt and may discard all support in about three months (Fig. 2). It is similar to the operations described by Breck and Basom[2] and Bosworth.[3]

Postoperative Course.—As a rule, the postoperative course is uneventful. An occasional patient has difficulty in voiding for a few days after the operation and catheterization may be necessary. A few patients convalesce slowly and require about three weeks' hospitalization. About 20 per cent of the patients complain of numbness in the side of the foot, which has sometimes persisted for several months. Absence or diminution of the ankle jerk on the affected side has persisted in several patients. This may be due to the novocain, to traction on the nerve root, or to preoperative damage to the nerve root by the protruding disc.

In a series of 120 consecutive operations for ruptured intervertebral discs there were three hematomas which were evacuated, two mild wound infections, and one severe wound infection. In the severe infection the patient developed a staphylococcus septicemia. In this patient the wound healed normally, the sutures were removed, and there was no evidence of local infection until the tenth postoperative day, but the temperature rose on the third postoperative day and the septicemia was

Fig. 2.—Postoperative lumbosacral fusion by using slab graft from ilium.

apparent a few days later. It is possible that this unusual course was due to the local sulfonamide in the wound. In spite of large amounts of penicillin the septicemia pursued a rapidly fatal course. The autopsy revealed no localized lesions except the wound and there was no evidence of meningitis, in spite of the fact that the dura had been torn slightly when it was dissected free from the protruded disc.

DISCUSSION

The results of the operation in my hands have not been as uniformly successful as I would wish. Some of my patients who have had definite discs removed are still complaining of pain and disability. One of these was re-operated and as no cause for the pain was found the spine was fused, but the pain has persisted. In two instances where a primary bone chip and Hibbs fusion was done at the time of the removal of the disc, reoperation with removal of the fused area on the affected side has resulted in complete relief in one patient and partial relief in the other, although nothing was found at either operation to explain the pain. Likewise, some patients in whom no pathology was found at the operation have been free from pain after the operation.

The explanation of failure to cure is not known. Undoubtedly, some of the failures are due to protrusion of a second disc which was not removed at the operation. Others are due to recurrence of protrusion of an incompletely removed disc. In others there seems to be a persisting neuritis in the involved nerve roots. In one patient treatment with deep x-ray therapy has been followed by partial relief.

In some cases compensation is a factor and operation in these cases is to be avoided unless the history and clinical findings are clear cut and the patient appears to be anxious to get well and return to work. It is more satisfactory to have the case settled and then let the patient decide whether or not he wants to be operated upon. It is very difficult to return these patients to a job involving manual labor as long as they are drawing compensation and trying to settle their claim. Much the same is true of enlisted men in the Armed Forces. Elective surgery on the enlisted man should be undertaken only after a thorough trial of conservative treatment and in most instances it is wise to place these men on limited service immediately and continue the conservative treatment while they are doing duty.

I do not believe that spinal fusion will result in relief of symptoms in many of the patients who have not been relieved by removal of the disc. I am now fusing fewer spines than I did two years ago and am no longer using bone chips over the open spinal canal after the ligamentum flavum has been removed, but prefer the notched plate graft described. I am not sure that the unusually thorough curettement used by Dandy[1] will result in fusion. The occurrence of Schmorl's nodes indicates that the interior of the vertebral body is very unstable if the osteocartilaginous plate is perforated or removed.

At present I know of no acceptable indications for fusion of the intact spine after the removal of a protruding intervertebral disc. In some clinics the spine is fused if a congenital anomaly is present, in others the spine is fused if the lumbosacral joints are considered to be unstable, and in others the spine is fused if hypertrophic changes are present. None of these are acceptable reasons for fusion. At present I do not

fuse the spine if a definitely abnormal disc has been removed, but reserve this operation for those patients with long-continued, chronic backache in whom the x-rays reveal a collapsed disc and in whom no pressure on the nerve roots is found and relieved at the operation. If spondylolischisis or spondylolisthesis is present, fusion is indicated if operation is indicated, but in these cases the spine is not intact and exploration of the disc is rarely indicated if the pain is relieved by rest in bed.

From what has been written here it is evident that we should continue to treat low back pain, with or without sciatica, conservatively and that we should reserve operative removal of the discs for those patients who do not respond to conservative treatment. It is also to be noted that the operation in its present state of evolution is not a completely satisfactory answer to the problem, but the same is true of most operations. In relatively few surgical conditions do we expect to cure 100 per cent of the patients of all of their symptoms by operation. When viewed in this light removal of a ruptured intervertebral disc is a sound surgical procedure if the cases are properly selected. When patients are not relieved by the operation, or when symptoms recur, the conservative treatment along the lines described should be used and they should not be operated upon until this has failed to give relief.

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CRANIOPLASTY WITH TANTALUM PLATE

Report of Eight Cases

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TANTALUM is a biologically inert metal in the sense that it does not corrode and does not irritate living tissue. It is the seventy-third element in the periodic table. Ekeberg, who discovered it in 1802, gave it its name because he found it tantalizing when he attempted to dissolve it in mineral acids. Despite its discovery over a century ago, it was not until 1940 that this metal was introduced for surgical use.[1] For the surgeon, particularly the neurosurgeon, it may prove to be the ideal metal, but sufficient reports of its clinical use have not yet been made to justify this conclusion.

Pudenz and Odom,[2] in the experimental study to develop a material which would prevent meningocerebral adhesions, reported absence of foreign body reaction and failure of development of adhesions between the cerebral and meningeal surfaces following the prolonged application of tantalum foil to the surface of the brain of cats. Pudenz[3] subsequently made an experimental comparison of the reaction induced by tantalum and silver clips implanted in the brain and meninges of cats. He found that the tantalum clips provoked minimal reaction, in contrast to considerable leucocytic infiltration following implantation of silver clips. Later, Pudenz[4] demonstrated the inertness of tantalum in animal tissue when he used tantalum plates to repair cranial defects in cats. Following removal of the plates with the surrounding tissue in one block, the plates were found to be enveloped in a delicate membrane which was adherent to the dura but easily separated from it, and the metal was found to be unchanged. There was neither inflammatory reaction nor osteoplastic inhibition at the edges of the defects and the capsules surrounding the plates were not of a progressive nature.

Since this work of Burke, Pudenz, and Odom, a number of neurosurgeons have been using tantalum to repair cranial defects. Fulcher[5] recently reported excellent results in one case. Penfield, Cone, and Spurling, in personal communications to Pudenz, have stated that they have used tantalum plates in the repair of cranial defects with uniformly excellent results. From personal communications we have learned that Army neurosurgeons are using tantalum almost exclusively for the repair of cranial defects. It is believed that 500 cases of cranioplasty with tantalum could now be assembled.

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Tantalum* is manufactured in the form of sheets, foil, ribbon, wire, screws, and orthopedic plates. Because of its widespread use in the manufacture of war material, it has only recently been released in limited quantity to civilian surgeons.

Among the physical properties of this metal which make it of surgical value are strength and malleability. In its annealed state it is ductile and can be drawn into fine wire, which makes an excellent suture material.

PREPARATION OF PLATES AND OPERATIVE TECHNIQUE

A tantalum plate can be laid on the skull so as to cover the defect completely (onlay method, Fig. 1, *A*) or it can be trimmed to the exact size and shape of the defect and inserted (inlay method, Fig. 1, *B*). For cranioplasty with the onlay technique a plate .0125 inches or less in thickness is desirable. The location and configuration of the defect in the skull should be noted. A sheet of metal should be cut to the approximate size and shape with tinsmith's shears and hammered to the correct curvature with a ball peen hammer. A skull should be available in the workshop as a guide. Many perforations should be made

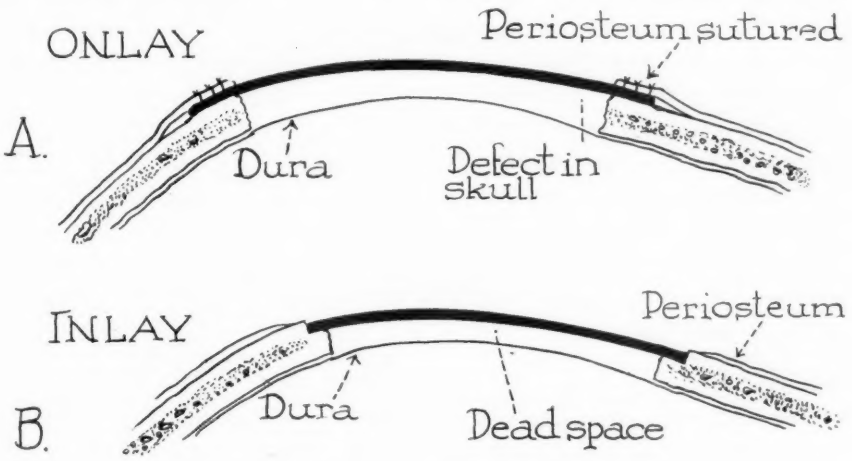


Fig. 1.—*A*, Onlay technique; *B*, inlay technique.

in the plate with a drill to facilitate suturing or wiring and provide for escape of cerebrospinal fluid and blood into the subgaleal space from which it may be absorbed or aspirated. Some observers state that a perforated plate is not desirable because the scalp is more apt to become attached to it.

At operation, under local or general anesthesia, the defect in the skull is exposed by reflecting a flap of scalp. The periosteum is retracted from the edge of the defect in the skull so that the metal plate can be laid in direct contact with the bone. If the plate is found to be too large, necessary alterations should be made with the shears. The plate

*Tantalum Defense Corporation, North Chicago, Ill.

should, of course, be somewhat larger than the defect in the skull. It is important that the edge of the plate be in contact with the surface of the skull if a palpable ridge is to be avoided. The periosteum is brought over the plate and sutured with cotton, silk, or tantalum. In case of an inadequate periosteum it is important to fasten the plate to drill holes in the skull by means of tantalum wire. A plate can also be secured to the skull with two or three tantalum screws. Migration of insecurely fastened plates has occurred. The scalp is closed in two layers with interrupted sutures of silk or cotton and a pressure dressing is applied.

Inlay Method.—The inlay method of cranioplasty with tantalum involves the making of positive and negative casts of the defect in the skull. The plate is then swaged into the desired shape. This method was demonstrated at the meeting of the American Academy of Neurological Surgery in Battle Creek in 1943 by Mayfield and Levitch and is presented in a motion picture made at the Walter Reed General Hospital. With a few special instruments the outer table of the skull is chiseled away around the entire periphery of the defect. This permits the plate to rest on the ledge formed by the inner table. The metal plate is flush with the surface of the cranium (Fig. 1*B*). The plate is firmly secured by driving several triangular tantalum wedges into the bone, much as a glazer secures the windowpane. If the cranial defect is on the forehead, the inlay method is especially desirable, as a slightly better cosmetic effect can be obtained.

The inlay technique is an excellent one but is not universally suitable because it is time consuming and expensive even though the material and equipment are available in dental laboratories. We have not used this technique and are reasonably well satisfied with the simpler one already described.

RESULTS

We have used tantalum plate to repair cranial defects in eight cases. Two patients had depressed fractures, recently healed. Three had old depressed fractures, complicated by convulsive seizures. Also included was a large defect of the frontal bone following osteomyelitis, which had been "cured" by surgical treatment. A case of parasagittal meningioma with exostosis at the vertex in which a large operative defect was repaired at the time of operation is presented. Another patient presented a compound fracture of the frontal bone with loss of the frontal sinus and roof of the orbit; there was displacement of the globe with diplopia. This case presented a difficult prosthetic problem because of the peculiar shape of the plate to be made.

In this small group of cases there were two complete failures. One patient (Case 4) returned to the hospital one year after operation on the frontal bone for osteomyelitis. A plate was applied but this was promptly followed by infection, whether because of defective aseptic

technique or as the result of stirring up latent infection by too early repair, we cannot say. In another patient (Case 1) the plate had to be removed one year later because of infection. This is difficult to explain, as there were complicating factors including the fact that the plate was inserted into a potentially infected wound. A more likely explanation is that the edge of the plate may have been elevated from the skull at one point with resulting erosion of the scalp. In the other six cases the plates have remained in place after periods ranging from two and one-half to fifteen months. In one of these (Case 6) the results are not entirely satisfactory because the patient complains of an intermittently sore scalp over the plate. This suggests the possibility that the plate may become hot when the patient is working in the sun. There is an untraceable rumor that cranial plates of tantalum absorb heat if the patient is exposed to sunlight or diathermy. The authenticity of this statement should be established before too extensive use of this metal is made.

CASE REPORTS

CASE 1.—I. L., a Negro, aged 47 years, was admitted to Charity Hospital in New Orleans, Jan. 22, 1943. Five days previously he was hit over the head by a car crank and was unconscious for two days. At the time of admission he was conscious and able to walk but was aphasic. Otherwise, neurologic examination gave negative results. On the left side of the head there was a scalp wound which had been closed by three sutures and was healing by first intention. Deep to this wound an osseous depression was felt. Roentgenograms revealed a depressed fracture of the skull involving the parietal and temporal bones. Feb. 2, 1943, eleven days after the injury, a small scalp flap was reflected downward over the ear. A trephine was made near the edge of the depressed fracture and all of the fragments were removed. One fragment had been driven through the dura. When this fragment was removed, an underlying artery on the surface of the brain began to bleed. In order to control this hemorrhage the dura was opened widely and then closed with interrupted cotton sutures. A perforated tantalum plate, which had already been prepared, was trimmed to the proper size and laid over the defect. It was fastened to the periosteum with several cotton sutures. Convalescence was complicated by bronchopneumonia which had cleared up by Feb. 6, 1943. The patient was discharged from the hospital Feb. 12, 1943. At reexamination, March 19, 1943, the wound had healed and the aphasia had completely disappeared. The patient had no complaints. In May, 1944, the patient returned to the hospital because the tissues around the plate had become infected. Inspection disclosed an ulcer of the scalp 2 cm. in diameter through which the plate could be seen. Pus escaped from the opening and the entire scalp flap was swollen. The plate was removed a few days later and the infection promptly subsided.

CASE 2.—E. L., a white man, aged 21 years, was admitted to Touro Infirmary Feb. 26, 1943, because of multiple contusions and lacerations caused by a fall. Two lacerations of the scalp had been sutured at a first-aid station; healing by first intention resulted. Roentgenograms of the skull made some days later showed a comminuted depressed fracture of the frontal bone. This proved to underly one of the healed lacerations. At operation, March 12, 1943, two weeks after the injury, a small scalp flap was reflected to expose a depressed fracture about the size of a quarter. A trephine was made adjacent to this and the depressed fragments were removed. The inner table was more extensively fractured than the

outer table. The dura was intact. A small amount of organized blood clot was also removed. A perforated tantalum plate, which had been prepared in advance, was laid over the skull defect and fastened to the periosteum with one cotton suture. The scalp was closed in two layers with cotton and a pressure bandage was applied. Convalescence was uneventful and the patient was discharged from the hospital on the eighth postoperative day. June 25, 1944, fifteen months after operation, the patient wrote that he was well and completely satisfied with the plate.

CASE 3.—F. B., a Negro man, aged 29 years, was admitted to Charity Hospital in New Orleans, June 4, 1943, because of jacksonian convulsions on the right side. He sustained a simple depressed fracture of the skull in October, 1940. In October, 1941, he began having frequent convulsions. There was a palpable depression of the left parietal bone. June 24, 1943, the skull was exposed, a trephine opening was

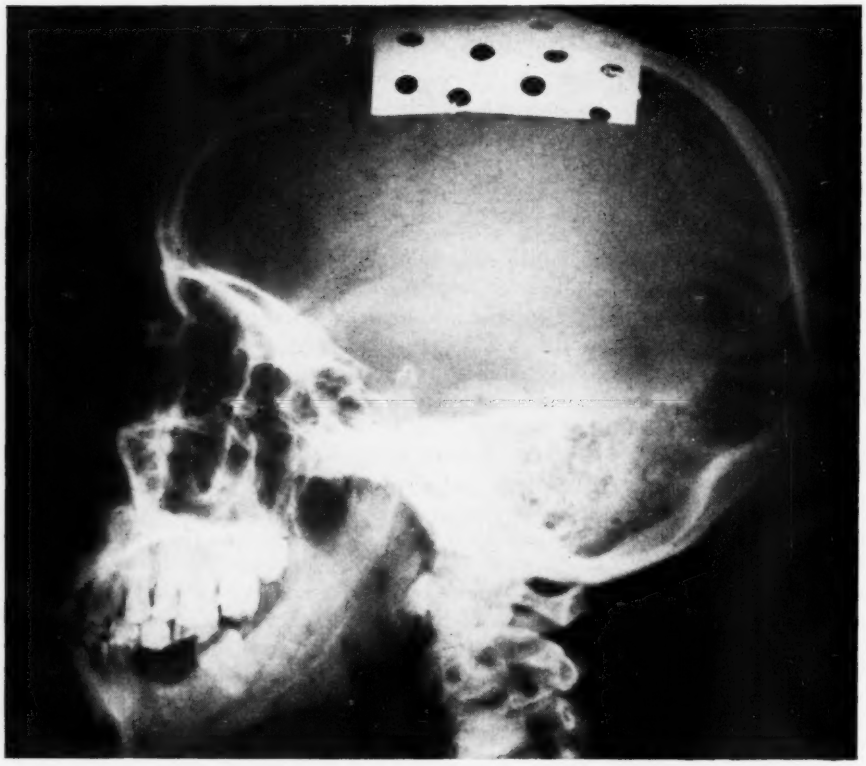
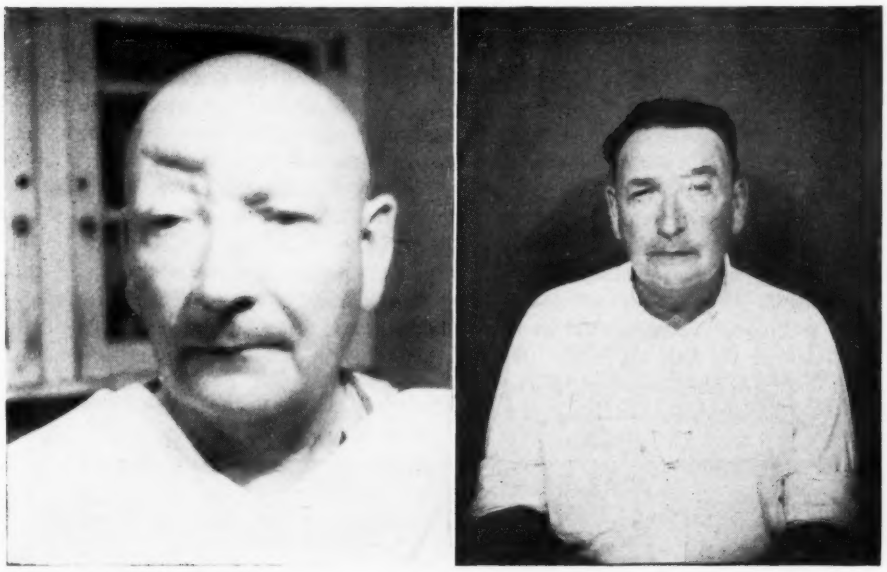


Fig. 2 (Case 3).—Postoperative view showing plate wired in place over defect.

made, and the depressed portion of the skull removed. One fragment of bone had penetrated the dura. The dural opening was enlarged to permit removal of this fragment; the brain appeared normal. A previously fashioned tantalum plate was cut to the correct size and wired in place over the defect (Fig. 2). There were no postoperative convulsions. The patient was discharged from the hospital, July 7, 1943, with instructions to take anticonvulsive medication for one year. He was drowned while swimming in February, 1944.

CASE 4.—J. H., a Negro boy, aged 16 years, came to Charity Hospital in New Orleans, June 28, 1943, because of a defect in the frontal bone. July 14, 1942, he was operated on for extensive osteomyelitis;* all of the infected bone, including

*Operation by Dr. Guy Odom.



A. *B.*

Fig. 3 (Case 5).—*A*, Preoperative photograph showing loss of supra-orbital ridge; *B*, postoperative photograph showing restoration of the supra-orbital ridge.

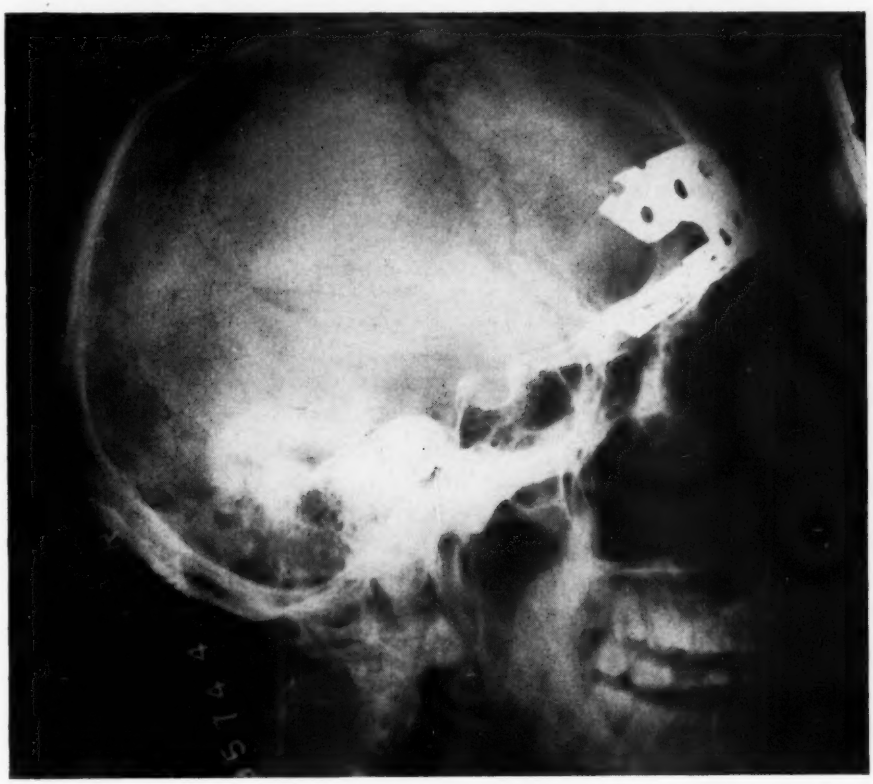


Fig. 4*A* (Case 5).—Lateral view showing reconstruction of roof of orbit and supra-orbital ridge.

most of the walls of the frontal sinus, was removed. Following an uneventful convalescence he was discharged from the hospital, Aug. 5, 1942. Roentgenologic examination, July 29, 1942, showed an extensive defect in the skull but no evidence of sequestra or infection. He returned to the hospital one year later to have this defect repaired. July 22, 1943, an incision was made through the scar of the old hypophyseal-type flap and the scalp reflected. After adequate hemostasis had been obtained, a previously shaped tantalum plate was laid over the defect. It fitted so snugly that sutures were not deemed necessary. The flap was closed in one layer with cotton sutures. July 24, 1943, there were 10 c.c. of serosanguineous fluid aspirated from beneath the flap. July 28, 1943, similar material, 50 c.c., was withdrawn. Culture showed *Staphylococcus pyogenes aureus*. There was little fever or pain. Attempts to save the plate were eventually abandoned and it was removed on Aug. 20, 1943. The wound was closed in one layer, and a rubber drain left in place. Convalescence was without incident and the patient was discharged, Aug. 23, 1943.

Fig. 4*B* (Case 5).—Postero-anterior view showing reconstruction of portion of frontal bone and supra-orbital ridge; the portion of the plate which forms the roof of the orbit is seen in Fig. 4*A*.

CASE 5.—J. P., a 51-year-old white man, was admitted to Touro Infirmary, Aug. 2, 1943. Nine months previously he had sustained a compound fracture of the right frontal bone which had healed following débridement. The frontal sinus, supra-orbital ridge, and part of the roof of the orbit were missing; this produced displacement of the eye and diplopia (Fig. 3*A*). No pulsations were noted. He

complained of numbness of the forehead, pain in the right side of the forehead, and double vision. A coronal incision was made just behind the hairline of the forehead and the scalp reflected over the eyes and nose. Sharp dissection was required to separate the scalp from the dura; no difficulty was encountered in separating the dura from the periorbita. A previously fashioned tantalum plate was trimmed to the exact size with tin shears and slipped into position to replace the missing supra-orbital ridge and the roof of the orbit (Figs. 4*A* and 4*B*). Following an uneventful postoperative course the patient was discharged from the hospital, Aug. 18, 1943. The original scar was repaired some months later. Reexamination in February, 1944, showed a satisfactory cosmetic result (Fig. 3*B*) and practically complete correction of the diplopia. However, the frontal pain still persisted.

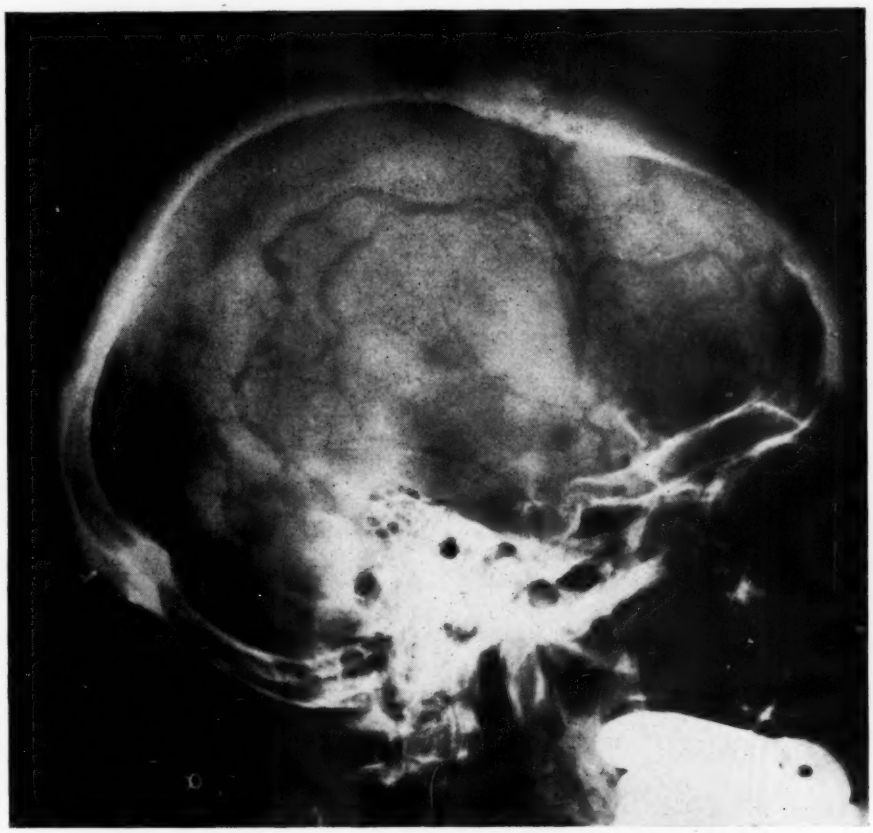


Fig. 5*A* (Case 7).—Preoperative view showing exostosis overlying parasagittal meningioma.

CASE 6.—E. C., a white man, aged 43 years, was admitted to Charity Hospital in New Orleans, Aug. 16, 1943. Twenty years before, he received a gunshot wound in the left temple from which he recovered except for mild aphasia. He was well until December, 1942, when he began to have headaches originating at the left side of the nose. Two months before admission he had a convulsion during which he was unconscious. Two weeks before he came to the hospital, he had another convulsion. Examination revealed the scar of an old wound in the left temporal region with a palpable defect at the same site. The scalp was adherent to the underlying tissues. Roentgenograms revealed the presence of a cranial defect and

numerous shotgun pellets in the soft tissues, some outside and some just inside the cranial cavity. Aug. 26, 1943, a scalp flap was reflected downward over the ear. The soft tissues covering the defect were dissected from the dura and the defect in the skull was enlarged to two inches in diameter. The exposed dura was excised with difficulty. Many adhesions between the brain and dura and many large vessels were encountered. A scarred area of brain one and one-half inches in diameter was noted with cystic spaces near the surface. Nothing was done to the scar because of its location for fear of making the aphasia worse. A previously shaped tantalum plate was cut to the correct size, laid over the defect, and wired into place. The patient was given 1½ gr. of sodium, 5,5-diphenyl hydantoinate (dilatin sodium) three times a day. Convalescence was uneventful. He had no convulsions prior to discharge from the hospital, Sept. 8, 1943.

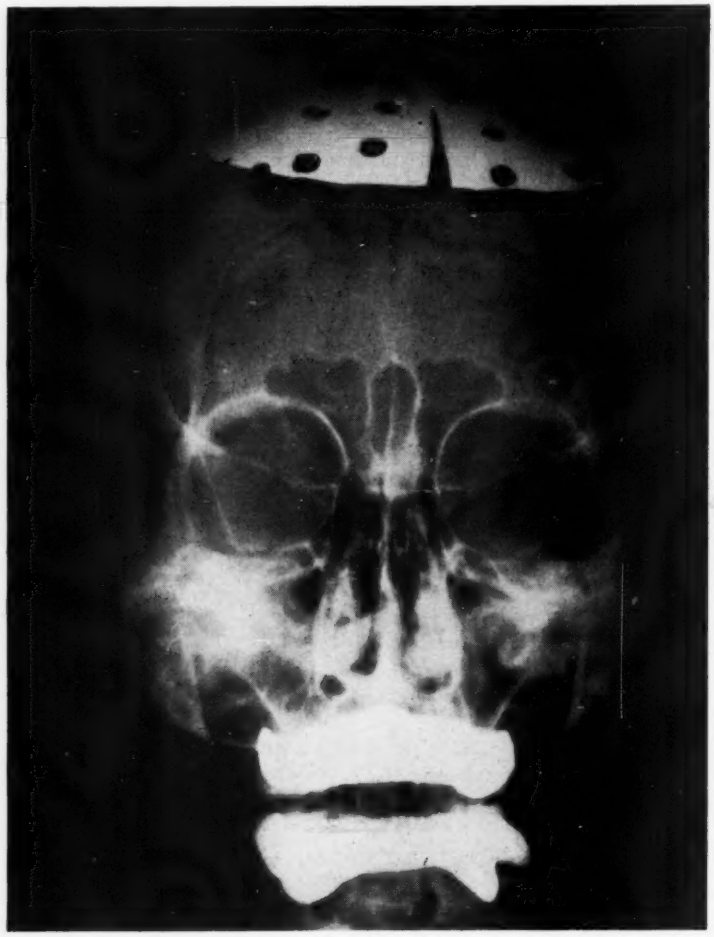


Fig. 5*B* (Case 7).—Postoperative view showing large tantalum plate covering operative defect.

April 26, 1944, eight months after operation, the patient wrote that he was free of convulsions but that he still suffered from the headache which had begun in December, 1942. The pain is apparently brought on by working two or three consecutive days on his farm. This point, together with the fact that the scalp over the plate becomes sore, suggests the possibility that the plate becomes heated. On the other hand, headache was a major complaint before insertion of the plate.

CASE 7.—S. P., a white woman, aged 62 years, was admitted to Touro Infirmary, Oct. 20, 1943, because of exostosis of the skull (Fig. 5*A*) accompanied by other evidence of a parasagittal meningioma. Oct. 26, 1943, a large U-shaped flap of scalp was reflected so that the hyperostosis and a margin of normal skull could be removed in one piece. A stalk of neoplastic tissue which connected the hyperostosis with a large parasagittal meningioma was broken with the finger. The dura was opened on each side of the sagittal sinus. On the left was a small meningioma which proved to be an extension (through the sinus) of the larger tumor. Both tumors, the adjacent dura, and the intervening sinus and falx were removed in one piece. The depressed portion of the right hemisphere promptly expanded. The cut edge of the dura was sutured to the periosteum around the entire periphery of the defect in the skull. A previously prepared tantalum plate was laid in place over the defect (Fig. 5*B*), the scalp was closed with cotton sutures, and a pressure dressing was applied.

At the time of re-examination, May 2, 1944, the patient was found to be in good health. She had regained the ability to walk, her personality had returned to normal, and the convulsions had ceased. At two places the edge of the plate could be palpated and the patient complained of tenderness. It was realized at the time of insertion that this was not a perfectly fitting plate.

CASE 8.—J. M. R., a white man, aged 56 years, was admitted to Touro Infirmary, Jan. 31, 1944, because of convulsive seizures and headaches. He had sustained a penetrating wound on the left side of the head at the age of 5 years. From the age of 20 until the time of a craniectomy at the age of 31 he experienced frequent severe convulsions with loss of consciousness. This operation (craniectomy at the site of the old wound and possibly excision of a meningocerebral cicatrix) was followed by temporary hemiplegia but it greatly diminished the frequency and severity of the convulsions. The patient had also had a prostatic operation, open drainage for empyema, and nephropexy.

Examination disclosed a cranial defect on the left side near the midline and about one inch back of the hairline. An encephalogram, made Feb. 1, 1944, showed moderate dilation of both lateral ventricles, the left being larger. There was slight tenting of the portion of the ventricle nearest the cranial defect. At operation, Feb. 5, 1944, the cranial defect measured 3 by 5 cm.; it extended to the midline. The opening in the skull was enlarged with rongeurs. The dura, which was firmly adherent to the brain, was excised to the margin of the sagittal sinus, dissected free, and discarded. The sinus was inadvertently opened at one point and had to be closed with a suture. There were no adhesions between the medial surface of the hemisphere and the falx. The brain scar was smaller than a dime and nothing was done to it, although it was probably far enough forward to have been removed without causing motor symptoms. A tantalum plate was laid over the defect and fastened in place with two tantalum wires. The periosteum and scalp were closed in layers. Feb. 10, 1944, some fluid, which had accumulated under the scalp, was aspirated with a needle and syringe. No convulsions occurred. The patient was discharged from the hospital, Feb. 15, 1944, with instructions to take sodium, 5,5-diphenyl hydantoinate (dilantin sodium) for one year. He was asked to come back for removal of the brain scar if the convulsions returned.

April 19, 1944, two and one-half months after operation, the patient wrote that he was working (watch repairing) and free of all head pain. He had experienced two light convulsive seizures without loss of consciousness and as a result had given up dilantin and gone back to taking phenobarbital, ¾ gr. three times daily.

SUMMARY

The properties of tantalum which make it a suitable metal for repairing cranial defects are enumerated and experimental evidence to

support this contention is cited. A technique of preparing tantalum plates for cranial defects is described. Eight cases in which tantalum plates were used to repair old or new cranial defects are reported. Satisfactory results were obtained in all but two instances, a case of osteomyelitis of the skull, which immediately became infected, and a compound fracture of the skull, not debrided at the time of injury, which became infected one year after cranioplasty.

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Editorial

Thrombo-Embolism

OPERATIVE treatment in all fields of surgical endeavor has been steadily improved due, in part, to the analytic study of complications and end results. It has been demonstrated that while the primary procedure might be correctly chosen and meticulously carried out, a fatal result was frequently due to secondary involvement of other organs and vital physiologic functions by disease processes initiated by trauma of operation, anesthesia, and other mechanics of treatment and convalescence. Pulmonary complications following operation have gradually been sorted out from the original ether pneumonia until a fairly satisfactory classification of their causes is now available. Aside from the activation of residual disease of bronchial tree and lungs by anesthetics, atelectasis as an important complication has been recognized. The frequency of occurrence and methods of diagnosis of this acute pulmonary complication are common knowledge and techniques for its prevention and treatment are well established.

It has long been known that pulmonary embolism was another not infrequent and often fatal complication of any operation. Many misconceptions pervaded surgical thought over the course of years concerning the origin of the thrombosis that initiated these emboli. Studies by many observers during recent years have finally clarified this problem and it is increasingly evident that most pulmonary emboli following operation have their origin in thrombi formed in the veins of the foot, leg, and thigh. It was originally thought that thrombosis in these veins started in the upper part of this venous system, in the femoral and lower iliac veins. Further studies by pathologists and clinicians have shown that thrombosis usually starts below the knee, frequently in the veins of the foot. From such a start, the process may advance to noninflammatory masses of thrombi in the femoral or iliac vessels called phlebothrombosis or to an obstructive inflammatory lesion known as thrombophlebitis.

The further local progress and distant spread of portions of the thrombi are variable but of important consequence. The etiologic factors favoring the origin of thrombosis have been widely studied and the importance of the many factors involved have been individually emphasized. Abnormalities in the clotting mechanism of the blood, anatomic and pathologic abnormality in the vein, and physiologic alterations associated with posture and lack of normal activity have all been mentioned frequently as primary or contributing factors. Both chemical and mechanical methods of prevention of thrombosis have their exponents.

Treatment ranges from bold operations to remove pulmonary emboli after their lodgment, to ligation of vein, aspiration of thrombus, and sympathetic block, to chemical methods of altering clotting time. Just as it is often difficult during a political campaign to keep before one the main issue, despite one's prejudices and the claims of opposing factions, so now, we as surgeons are faced with the difficulty of judging impartially the merits of the forms of treatment and the methods of prevention and treatment now advocated in thrombo-embolism arising in the peripheral venous system. The characteristic signs and symptoms of thrombosis in the peripheral venous system, many of the predisposing factors involved, and the characteristic manifestations of distant embolism calling the attention of the unwary surgeon to the presence of a frequently unsuspected thrombosis, have all been given recent prominence in surgical literature. One may safely say that frequent inspection of the lower extremity should become a routine in the care of all patients having undergone an operation. The recognition of early thrombosis is a necessity to the proper treatment, no matter what type of therapy may be chosen.

A state of indecision always arises when more than one form of therapy in prevention and treatment is available. Medical progress is based on the amassed statistics of groups or individuals vigorously championing one or the other form of treatment. The problem of thrombo-embolism is at present in this stage. Statistical studies are being compiled in favor of ligation of large veins of the extremities or of the trunk to prevent distant emboli and further progression of thrombosis in these veins. With a similar end in view, enthusiasts for anticoagulant therapy in this same group of patients are presenting a formidable showing in the current literature. There is no doubt but that sympathetic block overcomes the vasospasm and thereby aids recovery when such vasoconstriction is present. This state of affairs in which different methods of treatment have merits receives our cordial and enthusiastic encouragement. Truth of deduction can come only from intensive studies of all methods. We are no longer ignorant of the source of the majority of pulmonary emboli. The conservative methods of prevention by encouraging normal physiologic forces of venous flow by exercises and voluntary activity in bed and early postoperative mobilization after operation can elicit little antagonism. What then shall we do for those patients who, despite conservative preventive measures, develop evidence of peripheral venous thrombosis? This question will be answered on the basis of the comparative statistics compiled from the studies of those now at work in the field.

How can we judge the merits of the available forms of treatment? If one keeps in mind certain precepts one may be able to judge well for his patients. The formation and propagation of thrombi in the vascular tree must be prevented by promoting normal physiologic proc-

esses; if the process is initiated it must be stopped. The measures used by the surgeon must be simple, readily available, and effective. The treatment of thrombo-embolism as a complication must neither affect adversely the primary disease nor interfere nor complicate the treatment which is essential to this disease. The morbidity and mortality associated with the accepted therapy must be minimal. When these criteria are fulfilled, the problem of thrombo-embolism will no longer be a problem. The primary fact of source is now known. It is possible to extend prophylactic methods universally. Its early recognition is dependent upon simple clinical examinations. The numerous investigators in the field of treatment are urged to continue along their divergent lines of research and therapy until the analyses of their efforts will give the final truth.

—Frederick A. Coller, M.D.
Ann Arbor, Mich.

Book Reviews

The Neurosurgical Patient: His Problems of Diagnosis and Care. By Carl W. Rand, M.D. Cloth. Pp. 576, with 121 illustrations. Springfield, Ill., 1944. Charles C Thomas, Publisher. $4.

The growth of the field of neurosurgery from one concerned chiefly with attempts at removing neoplasms of the brain and spinal cord to one encompassing both anatomic and physiologic disorders of the nervous system at all levels is well illustrated by this volume by one of the Pacific Coast's leading neurosurgeons. In it, in addition to extensive discussions of the several varieties of brain and spinal cord tumors and of the near and remote effects of skull and spine injuries, one finds briefer consideration of the surgery of the peripheral and sympathetic nervous systems, of infections of the nervous system amenable to surgical management, and of such problems as the relief of malignant exophthalmos and spasmodic torticollis.

Each of the fifty-four chapters appears to be a more or less literal transcription of a clinical discussion presented by the author before groups of physicians or medical students. Each is introduced by a pertinent quotation from the older literature and the various problems discussed are accompanied by illustrations of patients from the author's experience. This, together with the conversational literary style, makes for easy, pleasant reading. However, the material is loosely organized and repetitions are frequent. Particularly annoying are the references to roentgenograms and diagrams which were displayed to the original audience but which are not reproduced for the reader. The details of surgical technique are not described.

The result is a book which will provide interesting reading for the physician curious about neurosurgery, but one which is not adequate as either a text or reference work.

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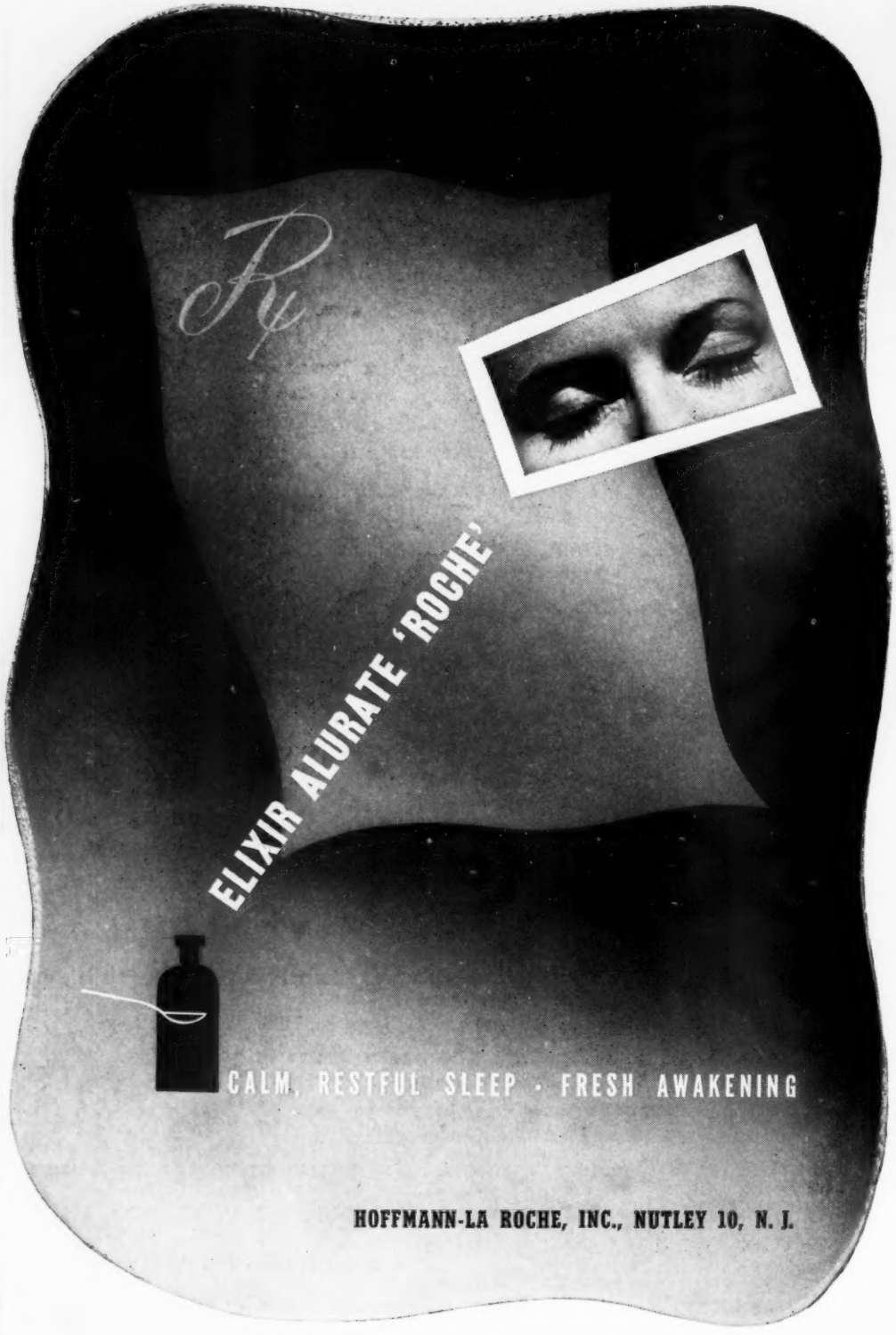
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